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ACUTE PERIPHERAL ARTERIAL OCCLUSION AND ITS TREATMENT*

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SINCE the first report of a successful embolectomy by Mosay and Dumont,[9] in 1911, there have been numerous articles published on peripheral embolism and its treatment. The percentage of extremities saved by embolectomy is still relatively low. In 1933 Pearse[11] reviewed the results of 282 embolectomies to find that 85, or 30 per cent, showed successful results. This finding is in accord with most statistics, although some small groups of cases may show successes as high as 40 per cent. New advances have been made in the treatment of peripheral arterial embolism since that report.

The purpose of this paper is to discuss present methods of treatment and to report an improvement in the percentage of extremities saved by the use of negative-positive pressure (Pavaex) therapy. The data for this paper have been drawn from a study of 44 cases of acute arterial occlusion occurring in 36 patients who were treated at the Massachusetts General Hospital from 1929 to 1936, including 1 case reported by Allen[1] in 1929 from the same clinic.

In this group of patients there were 40 cases of embolic occlusion and 4 cases of acute arterial thrombosis. It is worth noting that in a study of the histories of these two types of cases it is impossible to differentiate them. Thus, either embolism or thrombosis may produce acute arterial occlusion. This agrees with similar findings by McKechnie and Allen.[8]

The successful outcome of any form of treatment of acute arterial occlusion depends on the early diagnosis of the condition, followed immediately by proper treatment. If the limb is to be saved, there are few conditions that require a more rapid mobilization of therapeutic measures. It is truly an emergency in every sense of the word. Therefore, it seems to me worth while at this point to review briefly the symptoms and signs of an embolus and the method of localizing it.

SYMPTOMS

It is generally thought that the most characteristic symptom is sudden excruciating pain in the affected limb. This is not always the case, however. Thus, in 30 patients whom I have studied, only 20, or 67 per cent, gave a history of sudden severe pain. In the other 10, or 33 per cent, the pain was not of this character. Three patients had gradually increasing pain, 4 had numbness followed later by pain, and 3 did not complain of pain. These were all cases of embolism, either proved by operation or by pathologic examination. From these data, it is obvious that embolism cannot be ruled out because of the absence of sudden excruciating pain. This corroborates the report by McKechnie and Allen,[8] who found that pain was the initial symptom in only 54 per cent of the cases they studied.

The other symptoms which are more constant, providing the embolus lodges in the brachial or popliteal artery or at a point nearer the heart, are numbness of the involved extremity, paralysis of the more distal groups of muscles in the affected limb and coldness of the skin.

SIGNS

The objective signs are pallor, a decrease in the skin temperature, complete or partial anesthesia, absent skin and tendon reflexes, and no pulsations in the arteries peripheral to the site of embolism.

TREATMENT

An arterial embolus almost always lodges at one of the major bifurcations of the arterial tree. This is because the diameter of the arterial lumen diminishes abruptly at such points. The number of sites for such lodgment are, therefore, relatively few. If the leg is involved, the embolus may lodge at the bifurcation of the aorta, the bifurcation of the common iliac, the bifurcation of the common femoral or in the popliteal artery. In the case of the arm, the embolus may lodge in the axillary artery or at the bifurcation of the brachial artery at the elbow. Embolism in more distal arteries rarely produces serious damage to an extremity.

With the above possibilities in mind, the localization can be readily effected by careful palpa-

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tion of the peripheral blood vessels to determine at which point pulsations cease. If there is difficulty in locating this point by palpation, it is possible to determine it accurately by means of the ordinary sphygmomanometer. This method is helpful especially if the patient's legs are very stout. Thus, with the cuff inflated to a little above diastolic pressure, one will notice over patent arteries of the extremity a definite oscillation of the needle of from one-half to one division on the scale. A similar application of the apparatus below the site of an embolus will give absolutely no oscillation.

In general there are four main types of treatment: (1) embolectomy, (2) the use of intermittent negative and positive pressures, (3) the use of vasodilators and (4) symptomatic or "watchful waiting."

Embolectomy. The actual technic of embolectomy has been described adequately many times so that I shall not review it, but refer you to the literature (Allen,[1] Pearse[11]).

As already stated, the percentage of good results following embolectomy is too low. The following analysis of cases will help to explain the reason for the small number of saved extremities. Our series contains 12 embolectomies, which were done during the past 8 years.

TABLE 1. *Results in Cases Treated by Embolectomy.*

Location of Embolus	No. Extremities	Extremities Saved	Extremities Not Saved	Died Too Soon
Aorta, Bifurcation	1		1	
Common Iliac	4	1	1	2
Common Femoral	5	2	2	1
Popliteal	1		1	
Axillary	1	1		
Total	12	4	5	3

Table 1 gives the location of the emboli and the fate of the extremities involved.

The circulation was restored in 4 of these 12 cases. In this group there were 2 femoral cases, operated upon by Dr. A. W. Allen and Dr. L. S. McKittrick, respectively. The other 2, one axillary and one common iliac, were operated upon by the writer (figs. 1 and 2). The latter patient is alive and well 3 years following the embolectomy. In this group of successful cases, the operation was done not later than 4 hours after the lodgment of the embolus. Furthermore, the site of the embolus in each of the 4 cases was carefully determined, and the operations were directed toward an actual visualization of the artery at the point of obstruction. These facts clearly explain the reason for the good results.

Failure to localize the emboli preoperatively in 5 of the 8 unsuccessful cases played the most important part in the unsatisfactory results. Operation was performed in 4 of them within 2½ hours after the embolism and in the fifth within 8 hours. There was too long a delay between the onset of the embolism and the operation in 2 of the other unsuccessful cases. The eighth case proved to be one of acute arterial thrombosis in a patient 74 years of age. Such a condition is unsuitable for operation. Furthermore, because of the marked calcification of the arteries at this age, arteriotomy is usually contraindicated. The average age in this unsuccessful group was 49 years—only 1 year greater than that of the successful group.

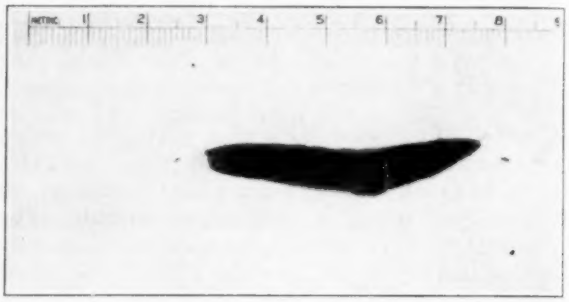

FIG. 1. Embolus removed from the left axillary artery within 1½ hours.

FIG. 2. Embolus removed within 3 hours from left common iliac artery.

Thus, improper localization and delay in operating explain the low percentage of saved extremities in 7 of the 8 unsuccessful cases.

Pressure Treatment. By means of mechanical devices it has been possible, within the past few years, to institute a new method of treatment for acute peripheral arterial occlusion. Credit is due Herrmann[6] and Reid,[12] and also Landis and Gibbon,[7] for this type of treatment. Each group has developed its own type of apparatus. The principle of both is essentially the same, namely, that the extremity with the occluded blood supply is exposed to alternating periods of negative and positive pressures in some form of airtight box. The difference, in brief, between the two apparatus lies in the fact that with the Herrmann-Reid type the negative and positive pressures are developed gradually, while in the Landis-Gibbon type the pressure changes are made rapidly. As to the relative merits of the two types of machines, I have no data.

In some of our cases we were forced to use

a modification of this type of treatment because of the breakdown of the machines that generated the positive and negative pressures. This modification consisted in using only negative pressure, which was obtained from the suction that is piped to all the hospital wards. To favor the return of the blood, the extremity was kept at a level above that of the heart. In order to have intermittent suction under these circumstances it was necessary to have someone close and open the suction line at set intervals. This was accomplished by inserting a T-tube in the suction line, so that with a finger placed over the open end of the tube, suction was produced, and on removal of the finger it was released. As the negative pressure is built up slowly by this means, it corresponds to the type of suction generated by the Herrmann-Reid apparatus.

The first case of acute arterial occlusion treated at the Massachusetts General Hospital by intermittent positive and negative pressures was in July, 1934. Since then until October, 1936, a period of 2 years and 3 months, 15 extremities on 13 patients have been treated by this method or by the modified method. In this group 9, or 60 per cent, of the limbs were saved; 3, or 20 per cent, were lost, and in the remaining 3, or 20 per cent, the patients died before the fate of the extremity was known (table 2).

TABLE 2. *Results in Cases Treated with Negative-Positive and Negative Pressures.*

Location of Embolus	No. Extremities	Extremities Saved	Extremities Not Saved	Died Too Soon
Aorta, Bifurcation	6	3	1	2
Common Iliac	1	1		
Common Femoral	6	3	2	1
Popliteal	2	2		
Total	15	9	3	3

These figures are very encouraging, especially so when it is realized that practically all these cases were unsuitable for embolectomy because of the general condition of the patient or the location of the emboli. In 2 cases the embolus was at the bifurcation of the aorta, in 1 case at the bifurcation of the common iliac, and in 2 others in the popliteal artery. Embolectomy should be a simple procedure from this latter vessel, but because of danger to the collateral blood supply about the knee, the exploration of the popliteal artery is fraught with more than ordinary risk to the extremity.

The findings at autopsy in 1 of the cases which were treated successfully with the pressure form of therapy were most instructive and encouraging in reference to the effect of the treatment. This was a case of embolism at the bifurcation of the aorta. Both lower extremities were saved despite a very marked arterial occlusion involving the arteries below the bifurcation of the aorta. Death was due to an embolism of the basilar artery in the skull about 1 month after the embolism had occurred in the aorta. The pathological report was as follows: "Beginning at the bifurcation of the abdominal aorta, there is a reddish-gray, moderately firm, friable, adherent thrombus, completely occluding the bifurcation for a distance of 3 cm. and extending into both the external and internal iliac arteries bilaterally. The thrombus in the right external iliac vessel extends for a distance of 6 cm. and stops at about the level of the profunda. The thrombus in the right internal iliac artery extends for a distance of 9 cm. The one in the left external iliac vessel extends for a distance of 17 cm. and also extends into the profunda." The pathological diagnosis was embolism and thrombosis occluding the bifurcation of the abdominal aorta, both right and left external and internal iliac arteries and the left profunda femoris artery. The diagram in figure 3 shows the location of the emboli and the thrombi.

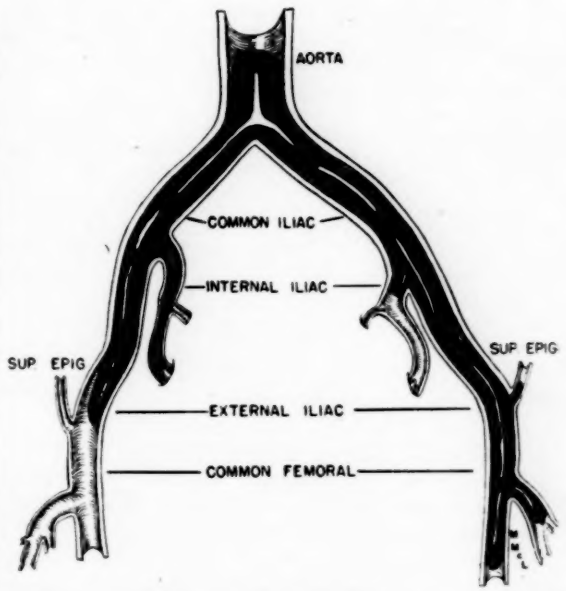

FIG. 3. Diagrammatic sketch of the aorta and its main tributaries in a case of embolism. Both legs were treated by the negative-positive pressure method, with restoration of the circulation in both extremities. Death was due to embolism of the basilar artery of the brain. (See text for full description.)

One of the important lessons learned from this case is the fact that, with the early application of the intermittent, negative-positive pressures, within 3½ hours sufficient blood was made to flow through the collateral channels to prevent the formation of secondary thrombi in the arteries distal to the points of occlusion. Thus, on the right, the superficial epigastric was found patent and opening into the femoral, as was also the profunda. On the left side, the collateral channels were not evident, as the bifurcation of the common femoral artery was oc-

cluded. A sufficient amount of blood apparently entered the left femoral artery lower down in its course, as all the arteries below the origin of the profunda were patent.

A comparison of the intermittent, negative-positive pressure type of treatment with that of intermittent negative pressure alone is given in table 3. This shows a definite advantage of

TABLE 3. *Results in Cases Treated with Negative-Positive and Negative Pressures.*

Type of Treatment	No. Cases	No. Extremities	Extremities Saved		Extremities Not Saved		Died Too Soon	
			No.	%	No.	%	No.	%
Negative-Positive	7	9	7	78	1	11	1	11
Negative	6	6	2	33	2	33	2	33
Total	13	15	9	60	3	20	3	20

the two phase type of treatment. Thus, 78 per cent of the limbs which were treated with the former method were saved, while the single negative phase method gave only 33 per cent good results. This difference probably was due not so much to the lack of positive pressure, as it was to the difficulty of maintaining the continuous application of the treatment for a long period, since the apparatus had to be run by hand instead of by machinery.

TABLE 4. *Good Results with Pressure Treatment.*

Location of Emboli	Age	Time Treatment Started	Duration of Treatment
Aorta, Bifurcation	47	3 hours	7 days
Aorta, Bifurcation	36	3½ hours	3 days
Aorta, Bifurcation	36	3 hours	3 days
Common Iliac	55	10 hours	7 days
Common Femoral	21	4½ hours	1+ days
Common Femoral	15	9 hours	6 days
Common Femoral	60	2 hours	5 days
Popliteal	33	24 hours	3 days
Popliteal	49	7 hours	6 days
Average	35	7 hours	4½ days

In tables 4 and 5 the good results and the failures are shown, respectively, along with the location of the arterial occlusions, the number of hours after the embolism that pressure treatment was instituted and the number of hours necessary to re-establish the circulation. From these data two important facts appear. First, the good results, with one exception, were obtained in the group of patients in whom the treatment was instituted soon after the embolism. Including all these cases, the average time interval was 7 hours. Excluding the 24-hour popliteal case this average time is decreased to 5 hours.

The second important fact is that the average age is less in the successful group of cases. This is as one would predict, since the arteries in a younger person have more elasticity, and as a result, collateral circulation can be more readily developed. The average length of treatment necessary to establish an adequate circulation was 4½ days.

Vasodilators. There are two important methods of producing vasodilatation, which should be mentioned. The interruption of the sympathetic pathways to the lower extremities has been shown by Mulvihill and Harvey[10] to have beneficial effects on experimental vascular occlusion in normal dogs. Theoretically, therefore,

TABLE 5. *Failures with Pressure Treatment.*

Location of Embolus	Age	Time Treatment Started	Duration of Treatment
Aorta, Bifurcation	47	3 hours	7 days
Common Femoral	45	5 hours	3 days*
Common Femoral	67	48 hours	Not stated
Average	53	19 hours	

*Treatment given inadequately.

this should be of help, especially in young persons with vascular occlusion. The best means of producing it would be by novocain or alcohol injection of the lumbar ganglia.

The second method is by repeated intravenous administrations of papaverine hydrochloride. There have been reports on the use of this drug by Denk,[4] Allen and MacLean[2] and deTakáts,[5] who have had varying degrees of success following its use.

Owing to the fact that we have attempted to evaluate the results of the pressure form of treatment alone, I have no data concerning the results of either method of vasodilatation. The important point to be stressed concerning the production of vasodilatation is that this form of treatment should not be used alone but in conjunction with embolectomy or with the pressure treatment. It is our purpose to follow out such a plan in future cases.

Symptomatic Treatment. Under this classification in our series there were 17 extremities. The results of treatment in these cases are shown

TABLE 6. *Location of Emboli and Age of Patients in Cases without Treatment.*

Location of Embolus	Saved	Age	Not Saved	Age	Died Too Soon	Age
Axillary	1	49				
Brachial	3	15 32 55	1	49		
Aorta, Bifurcation					3	49 51 51
Common Iliac, Bifurcation	1	26	1	59		
Common Femoral			3	26 54 54	1	59
Popliteal			2	61 64	1	68
Total	5		7		5	

in detail in table 6. It will be noted that 5, or 29 per cent, of this group were saved. These figures are misleading unless they are analyzed,

since four of the five emboli occurred in the arm. Excluding these 4 cases because of the frequency with which embolism of the arm improves spontaneously, the percentage of recoveries drops to about 8 per cent. In my opinion, there is nothing to recommend this course of treatment in acute major arterial occlusion, and I include it only for completeness.

SUMMARY

A series of 44 cases of acute peripheral arterial occlusion is presented. The symptoms, signs and method of localization of an embolus are reviewed. It is emphasized that the early recognition and prompt treatment of this condition are essential for success. There were three types of treatment used in handling this series of emboli. The results obtained are given in table 7.

TABLE 7. *Comparison of the Results of Different Types of Treatment.*

Type of Treatment	No. Extremities	Average Age	Extremities Saved No.	%	Average Age	Extremities Not Saved No.	%	Average Age	Died Too Soon No.	%	Average Age
Embolectomy	12	49	4	33	48	7	58	49	1	8	58
Negative-Positive Pressures	15	45	9	60	40	3	20	56	3	20	52
No Treatment	17	42	5	29	35	7	41	50	5	30	57
Vasodilators	0										

One group of 17 cases received symptomatic treatment. Five extremities did not develop gangrene. Four of these five had emboli in the arm. Adequate collateral circulation develops spontaneously very frequently in embolism of the upper extremity. In 5 arm cases seen in this series of 44 cases, 4, or 80 per cent, recovered without treatment. Excluding these 4 there remain 13 cases, only 1, or 8 per cent, of which was saved. Thus, there is nothing to recommend this method of handling peripheral embolism.

Embolectomy was done in 12 cases. Four, or 33 per cent, of the extremities in this group were saved. This figure compares favorably with other reports of embolectomy in the literature. The operation, to be successful, should be done at the earliest possible time after the embolism, preferably within 6 hours. The operation should be most successful on patients under 50 years of age because the arteries are not so apt to be calcified.

Fifteen cases were treated with the negative-positive pressure apparatus (Pavaex) or with intermittent negative pressure. In this group 9 extremities, or 60 per cent, were saved. This is the highest percentage of extremities saved that has been reported by any one method of treatment. It is worth noting that most of the latter cases were not suitable for embolectomy. The best results were obtained when the treatment was instituted early, within 3 hours after the embolus lodged. The younger patients developed an adequate collateral circulation more rapidly than did the older ones. This method of treatment is especially adapted to patients whose condition does not warrant operation. It also is recommended to be used following embolectomy.

CONCLUSIONS

1. A series of 44 acute peripheral arterial occlusions has been presented.
2. These cases were divided into three groups according to the method by which they were treated.
3. The use of the negative-positive pressure method of treatment gave the highest percentage of good results; it was 60 per cent successful in a group of 15 cases.
4. The writer believes the ideal method of treatment for suitable cases is a combination of treatments, namely, embolectomy followed by use of the pressure treatment and also the production of peripheral vasodilatation.
5. The early diagnosis and immediate treatment are the sine qua non of a successful outcome.
6. In cases properly treated there should be a still higher percentage of saved extremities.

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WHY MEDICAL SERVICE COUNCILS?*

A Report to the Public Relations Committee, Massachusetts Medical Society

THE Council of the Massachusetts Medical Society at the meeting in Springfield on June 9, 1936, voted to adopt the recommendations of the Public Relations Committee: that medical service councils consisting of carefully chosen representatives of all professional groups offering medical service—public health and welfare departments, health associations, and so forth—be formed in each district society area; and that a central council be formed for the State at large, which would be in effect a research body in medical economics and legal relations and would have an advisory and coordinating relation to the local organizations. The full text of the vote was recently published in the *New England Journal of Medicine* (**215:** 179 [July 30] 1936) and may be read or reread by all who are interested in the economic problems relating to medical service, and who wish to see the medical profession assume the guidance of whatever new plans are put into effect in the interest of more widespread and effective distribution of the benefits of modern medical service.

The Public Relations Committee put forward the plan for medical service councils because of its recognition of impending changes in our social order as well as of conditions which affect adversely the adequacy of medical service under our present system—points which have perhaps been factors in the genesis of the demand for such panaceas as compulsory health insurance, state medicine, and so forth.

At a special meeting of the Council of the Society held on April 4, 1935, when the studies on adequacy of medical care were authorized, the resolution carried with it a pledge to find and apply remedies for such inadequacies as should be revealed by the investigation.

The information now at hand constitutes a challenge to the Society to take such steps as seem possible to redeem that pledge.

In the preamble to the recommendations adopted by the Council last June, certain characteristics of our system of medical service which result in inadequacies were briefly summarized. Of these, four seem susceptible to relief or betterment by intelligent effort on the part of the medical and allied professions with the cooperation of various other agencies having to do with health and welfare problems. These are: (1) inadequacy of our laws governing the licensure of physicians; (2) defective distribution of medical facilities and practitioners in relation to the distribution of the population; (3) lack of information as to medical services obtainable and failure to recognize their own needs on the part of the people; (4) the so-called "economic barrier", which results in neglect to secure needed medical care or supplies because of inability to pay for it.

Let us consider these points in more detail.

1. *Inadequacy of Our Laws Governing Licensure of Physicians.* When seeking to correct evils of any kind, it is the part of good sense to begin by attacking those nearest home. It did not require a microscope to discover that adequate medical service could not be expected as long as the body of licensed practitioners in Massachusetts was being recruited in increasing ratio from graduates of substandard schools both foreign and domestic. The Massachusetts Medical Society has adhered consistently for a generation to the basic principle of adequate educational qualifications for all practitioners of the healing arts. By virtue of its concentrated efforts during the past two legislative sessions, under the leadership of Presidents Robey and Mongan, there has finally been written into our statutes a provision whereby the standards of medical education acceptable in this state can be defined and fixed by a special board consisting of the commissioners of education and public health and the secretary of the Board of Registration in Medicine. If the officials who are to constitute the board continue to be of the high type to which we have grown accustomed, and which we have a right to expect, the achievement will gradually redeem the Commonwealth from its unenviable distinction as the "most backward state" in this regard.

On this count we may fairly claim to have taken a notable step toward the fulfillment of our pledge of April 4, 1935.

2. *Defective Distribution of Medical Facilities and Practitioners.* At a meeting of the committee on January 22, 1936, a series of maps were presented which depicted the distribution of doctors, general and special hospital beds, and the population by counties throughout the state, the figures being derived from the *Journal of the American Medical Association* (**104:** 1075 [Mar. 30] 1935), the Massachusetts Medical Society *Directory*, and similar authentic sources. Among the striking figures we quote the following:

Massachusetts stands fifth among the states in ratio of general hospital beds to population,

*Submitted September 23, 1936, by the Subcommittee on the Adequacy of Medical Care: Dr. Ernest L. Hunt, Worcester, *Chairman*, Halbert G. Stetson, Greenfield, and Dr. Patrick J. Sullivan, Dalton.

having one bed for each 221 persons. Ohio's ratio is 1:375 and Mississippi's 1:700. While the Massachusetts average is high, the ratio per county shows a variation equal to that by states, Suffolk having 1:130, Essex 1:436 and Plymouth 1:703. The rate of occupancy in Massachusetts was 70 per cent. General hospital beds totaled 17,172.

The distribution of licensed practitioners varied similarly. The state averaged one doctor to 651 people. Of the counties, Norfolk had the highest ratio, 1:297, while Worcester had but 1:783, Franklin 1:973 and Dukes 1:1476.

Now, interestingly enough, comes a study, apparently by a member of the editorial staff of the *Journal*, based upon the recently issued *American Medical Directory* and the 1935 census (see *New England Journal of Medicine* [**215:** 406 and 412 (August 27) 1936]). This study shows that the general ratio of doctors to population for the State has increased to 1:597. The writer states that in 10 years there has been an increase of 17 per cent in number of doctors while the population increase has been less than 5 per cent. Nevertheless, 84 towns with a total of 80,399 population are without doctors, though not necessarily without medical service. Among towns of less than 5,000 population, Dighton with 3,116 people, has but one doctor, while Warwick, with 565 people, has two doctors.

Of course, modern roads and vehicles do much to offset these inequalities in distribution of doctors and hospital beds, but with the doctors increasing so much faster than the population, a more scientific placing of the newcomers would seem to offer one method to overcome the handicap of rural life so far as it relates to medical service. Active and effective medical service councils could deal understandingly with these problems by promoting popular demand for good doctors and drawing such to the localities in need. In the meanwhile, the central council might see fit to conduct an information bureau for the guidance of new licensees seeking opportunities to locate, or to seek modifications of the law to prevent overcrowding.

While it is not the mode just now to invoke the spirit of the N.R.A., the logic of events may call for numerical as well as educational limitations upon those who would enter upon the practice of medicine within the Commonwealth. If the population curve flattens out or descends, the medicoeconomic problems will become correspondingly acute. *For the present, the problem is to convert a quantitative numerical adequacy of physicians to an available adequacy of medical service.*

A time of financial depression like the present, when many hospitals are operating with large deficits and are striving to devise new plans of financing hospital care, would seem opportune to set about correcting the wastes of money and human effort which result from the overlapping of medical service facilities of various types, particularly hospital service.

The reason for the founding of most hospitals other than those supported by public funds has usually been some kindly urge for humanitarian service. Religious orders, racial groups, fraternal societies, individuals wishing to endow living memorials, all have seen in the hospital a practical expression of their will to serve humanity. Generous impulse, rather than careful estimate of community needs, accounts for a large percentage of the endowed and nonprofit association hospitals. What wonder that they are not located for maximum efficiency and overlap rather than supplement each other in type of service rendered. If medical service councils had no other challenge to their usefulness, this situation alone would justify their being.

3. *Information for the People.* So much is written for lay consumption in magazines and the daily press upon health and related subjects that it seems hardly believable that people can still be indifferent to and ill-informed upon matters of such vital importance to themselves and their dependents as the sources of medical service and how to secure it in time of need. The State Cancer Clinics are constantly bringing to light neglected cases of real cancer, and every one of us frequently runs across serious diseases and conditions which might have been cured or corrected had earlier opportunity been afforded.

Under our revered institution of personal liberty the initiative in seeking medical care lies with the individual in need of it. Therefore, enlightenment of the individual as to his health needs is of importance hardly secondary to the provision of adequate facilities for medical service.

Campaigns for lay education in the possibilities of preventive medicine and the importance of early diagnosis have been of great importance in the control of tuberculosis and diphtheria. A committee made up of persons representative of the various professional groups, and welfare and health organizations, would not be under the same inhibitions as regards publicity that apply to the Society itself, and could teach these things more effectively. Many other deficiencies in the public understanding of health matters suggest themselves. The proper and legitimate use of hospital facilities and specialists' services, value of immunizations and how to secure them and dietary fads and abuses are some of the possibilities of an educational program.

4. *Neglect to Secure Needed Medical Service Because of Inability to Pay For It.* Among the 500 families interviewed in our survey upon adequacy of medical care, 75, 15 per cent, admitted the need of medical care which was not

had by reason of financial disability; 101 families, 20.2 per cent, admitted need of supplies, appliances, and so forth, which were not had for the same reason; 150 families, 30 per cent, admitted need of dental service which they felt unable to afford; and 22, 4.4 per cent, needed nursing service which they could not pay for. We have the testimony of everyday experience to bear out the returns from both the questionnaire to doctors and the survey of population to the effect that the economic barrier is the chief obstacle between the individual citizen and adequate medical service.

Our conception of the remedy for this was offered at the meeting of this committee on April 1, 1936. Discussion of the plan by a group of Worcester doctors brought from a leading advocate of state medicine the comment, "It is the only way, if we are to preserve the status quo," meaning our present general system of medical service. Lest the details of the plan have been forgotten, we quote from that report:

"We suggest a plan for reorganizing the medical service on the basis of small hospital units in the small centers of population supported jointly by the community, assisted where necessary by State funds, and State supervised through a council of experts from the State societies and the Department of Public Health; each hospital to be a health and welfare center open, under proper regulations as to type of work to be done, to all qualified doctors. Medical care of the indigent and the near indigent ("medically indigent") to be paid by welfare departments pro rata as agreed upon by the community and the medical societies. Dental, nursing, and social service, as well as medical, would be under the health center; and in each locality a health council made up of persons from the various professions and welfare bodies would govern the policies and promote the service of the center.

"In this State, it is probable that little or no new building would be required, since fairly adequate hospitals exist in most communities. It is the method of organizing their service that would be new; and some changes in our laws governing the use of welfare funds and the administration of welfare relief in general would have to be brought about. In the great cities, redistribution of medical facilities on the principle of health centers could gradually be brought about, and the special needs of the medical schools for clinical material and of the well-to-do for private service would be recognized. For the group of people above the indigent but below the well-to-do a system of voluntary insurance, guided and administered by the medical and dental societies and hospital associations, seems rational and workable. Compulsory insurance would be taxation disguised by another name, and would erect a costly structure of administration and likely become a political football. Let us call a tax a tax, and promote health service by proper use of welfare funds under expert central guidance but decentralized management by boards not under direct political control.

"These changes in our system, we think, might be gradually developed on the basis of present facilities and organization with little disruption and loss. The difficulties would be: first, to secure broad legislation necessary with the repeal of laws which would inhibit such a development; secondly, to bring the various agencies into harmonious and cooperative relations; and, thirdly, to find and clothe with adequate authority persons able and big enough to develop the plan."

In the event that advance toward the plan promulgated at that time becomes an objective of our efforts, the medium of local and general medical service councils would be of great utility, and should become the administrative groups in charge of the health centers ultimately set up. Our thanks are due Dr. Channing Frothingham for so nobly espousing the cause of "community hospitals" in his speech at the annual meeting of the Harvard Medical Alumni, September 15, 1936.

Other Constructive Functions of the Medical Service Councils. It is our belief that one of the best immediate objectives for the work of all such councils would be to sell the idea advanced by the Subcommittee upon Public Health and Practitioner Relations and adopted by the Council on June 4, 1935. Item 4 states, "That the indigent sick in any community in the Commonwealth should be cared for by the individual physician through the proper authorities." This ideal has been achieved in Franklin County and in various townships in other counties. Could it become universal, it would go far to solve the problem of adequate medical care for the indigent, would spread the cost of such service over all the community, and would awaken the public to a decent appreciation of the idea that, if good medical service is wanted, it should be paid for like any other commodity or service. With this as a stepping-stone, other elements in the program could gradually be established.

The prepayment plan for hospital service, to the principle of which the Council has committed itself upon our recommendation, will need such bodies as medical service councils to popularize it and to guide its destiny after it is established. Should a similar plan for medical service eventuate, they again should be the mediums for its effective application.

Abuses of medical charity through the use of hospital facilities, intended for the poor by those

able to pay for medical care might well be subject to investigation and correction through the influence of the local councils.

This résumé has barely scratched the surface of the fertile fields for usefulness of such councils. We believe that the Massachusetts Medical Society should proceed actively to the task of organizing and setting them to work.

Your attention is invited to the following comment from the editorial pages of our *Journal* (**215:** 207 [July 30] 1936):

"That (the report) of the Subcommittee on the Adequacy of Medical Care is important. It outlines the need for education of the public and the profession through medical service councils and suggests methods of approach to important problems in order to improve existing conditions.

"How far the work of the Committee will be productive depends upon the effective interest shown in this report by the members of the eighteen District Societies.

"Active and compelling leadership will promote the success of the plans by worthwhile organization of service to the people. If, on the other hand, no cooperation on the part of the general profession is forthcoming, the recommendations will be sterile. If the usual lethargic habit of a large proportion of the profession persists, nothing will be done. Some will watch with interest for the awakening of a more general and practical endorsement of the report of this Committee."

THE METABOLIC BACKGROUND OF RICKETS

An Interpretive Review

BY RICHARD GUBNER, M.D.*

IT is a general axiom of medical investigation that the understanding of disease processes properly should precede and form the rational approach to prophylaxis and cure. In the case of rickets, however, the order is somewhat the reverse, for, while the prevention and cure of rickets have been well established in recent years, the underlying metabolic disorder is still imperfectly understood.

In any attempt to comprehend the pathogenesis of rickets, one must consider all the phases that recent investigations have brought to light and assign to each its proper part. Thus, not only must the structural changes in the bones, which constitute the obvious pathologic features of the disease, be considered, but due regard must also be given the disturbances in calcium and phosphorus metabolism and the roles of vitamin D, the parathyroid glands and the enzyme phosphatase. Inasmuch as the precise mechanisms of none of these factors have yet been ultimately settled, any concept grouping them all in a pathogenetic sequence can at best be considered suggestive and provisional.

RICKETS A DEFECT IN MINERAL METABOLISM AND NOT A PRIMARY DEFECT IN OSSIFICATION

Rickets, as well as osteomalacia, its counterpart in the adult, may be defined as a derangement of mineral metabolism due to vitamin D deficiency, which is frequently associated with inadequate calcium or phosphorus or both in the diet, leading to characteristic osseous changes. This concept, although generally accepted, is not shared by all. Pick,[1] for example, recently summarizing his own views and those of such authorities as von Recklinghausen and Schmidt, concluded "that the nature of rickets and osteomalacia may be found in a primary diseased condition of the bone tissues. Disturbances in calcium or mineral metabolism at best can be considered to have a parallel coordinated course with respect to the pathogenesis of rickets and osteomalacia, being in no way, however, the dominant feature."

Although many have considered the action of vitamin D to be directly concerned in bone metabolism, it has become increasingly apparent that vitamin D does not exert its effect on bone and that the calcifying mechanism per se is not impaired in rachitic bone.

In vitro experiments by Harris,[2] in collaboration with Robison, failed to adduce any evidence of "stimulation of calcification for the vitamin itself acting directly on bone." Howland and Kramer[3] in 1921 first demonstrated that the impaired calcification in rickets is due to a reduction of the bone-forming minerals in the tissue fluids rather than to an inherent defect in the bone; a diminution of serum phosphate and, to a lesser extent, of serum calcium was found regularly in active rickets. With institution of therapy the concentrations of these elements rise to normal values, and calcification takes place. In 1924 Shipley[4] reported that, on placing slices of the cartilage and bone of a rachitic rat in the serum of a normal rat, calcification occurred in a similar manner to that taking place in a living rat fed on a curative diet. Shipley, Kramer and Howland[5] further observed that slices of the cartilage and bone of rachitic rats became calcified in a normal manner when placed in sterile solutions of inorganic salts with calcium and inorganic phosphate concentrations approximating those found in plasma. This work was confirmed by Robison and Soames.[6]

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ROLE OF VITAMIN D IN MINERAL METABOLISM

The reduction of serum phosphate and calcium in rickets is due to an inability of the body to hold the normal quantity of these substances, and the action of vitamin D is directly concerned in the preservation of the mineral balance. In active rickets there is a diminished retention of calcium and phosphorus; and, with the administration of vitamin D in the form of cod-liver oil or irradiated ergosterol or by increasing its content in the body by ultraviolet irradiation, the retention of calcium and phosphorus returns to normal. This was first shown by Schabad[7] over 25 years ago and has been repeatedly demonstrated since by metabolic balance experiments.

Since vitamin D does not appear to act on bone and since it does not serve to increase the amount of calcium and phosphate that can be dissolved in serum (Harris[2]), its favorable effect on mineral retention must be sought elsewhere than in the bones or serum. The view entertained by many that vitamin D favorably influences the intestinal retention of calcium and phosphorus has been championed particularly by Bauer[8, 9] and his associates, and by Harris.[2]

Bauer, Marble and Claflin[8] found that vitamin D administered to normal subjects results in a fall in the fecal calcium and phosphorus, which is accompanied by a rise in the urinary calcium and phosphorus. The calcium and phosphorus balances are little affected. The authors interpret their results as showing that the action of vitamin D is to increase the intestinal absorption of calcium and phosphorus, and that vitamin D does not act in the body tissues to increase retention. In an accompanying communication, Bauer and Marble[9] conclude, "The action of irradiated ergosterol is the same in normal individuals as in individuals with calcium deficiency diseases, namely, to increase absorption of calcium and phosphorus from the gastrointestinal tract. If there exists a calcium phosphate deficiency of the serum, as well as the bones, the additional calcium and phosphorus absorbed is retained in order to establish a normal relationship of calcium and phosphorus in the serum and, thus allow the deposition of calcium phosphate in the bones."

Harris[2] states, "The effects of vitamin excess stand in logical contrast with those of a shortage, the mode of action of the vitamin in excess being essentially an intensification of its normal action when given in small amounts. . . . Just as vitamin D deficiency causes inadequate net absorption, low blood calcium and/or phosphorus and resulting inadequate calcification, so vitamin D excess, on the other hand, brings about a greatly increased net absorption, a tendency to hypercalcemia and/or hyperphosphatemia and excessive formation of densely calcified new bone."

Jones[10] and his associates found that vitamin D failed to raise the serum calcium of dogs deprived of calcium in the diet; whereas, if calcium was supplied in the diet, hypercalcemia resulted. These authors remark, "These data would indicate that the excess calcium of ergosterol hypercalcemia comes from the food, the absorption of which is increased under the influence of this drug."

It is difficult to dissociate calcium and phosphorus excretion, but the trend of evidence seems to indicate that the decreased mineral retention in active rickets is, more specifically, a diminished phosphorus retention, which secondarily carries out calcium with it as insoluble tertiary calcium phosphate. Schabad,[11] a pioneer in metabolic studies in rickets, found that not only are calcium and phosphorus in the feces both increased in absolute amount, but that the ratio of phosphorus to calcium excretion is greatly increased and may exceed its equivalent of calcium, although normally the fecal calcium is always greater than fecal phosphoric acid, for the calcium is bound not only to the phosphoric acid, but also to the fatty acids, with which it forms soaps, and to carbonates. Schabad concluded from this finding that "the prevailing opinion that phosphorus excretion depends upon the increase of calcium in the feces which serves merely to bind and neutralize the phosphoric acid was a misconception, indeed a reversal of the true state of affairs." This point of view is borne out by chemical analysis of the blood in rickets, which shows an almost normal percentage of calcium, whereas a marked diminution of inorganic phosphate in the blood is a constant finding; the reduction in inorganic phosphorus usually approximately parallels the intensity of the rachitic process.

McGowan[12] found a marked shift in phosphate excretion from feces to urine following large doses of vitamin D. In each of four rabbits, he observed a definite and consistent rise of blood phosphorus following the administration of vitamin D; the blood calcium was unaffected. He believes that calcium plays a secondary role to phosphorus and is affected only inasmuch as it acts to neutralize the excretion of phosphate ion. Other investigators have noted a rise in blood calcium as well as in phosphorus with the administration of vitamin D (Warkany; Crimm and Strayer; Jones and Rapoport; Ashford; Naser; Sobel, Goldfarb and Kramer; Harris and Innes).[13]

Stolzberg and Meyer[14] found that in rats that were on diets inducing rickets the blood phosphorus fell faster than the calcium early in the disease. Rominger, Meyer and Bomskov[15] found the same fact to be true in human rickets and regarded "rickets as a primary disturbance in phosphorus metabo-

lism." Kay and Guyatt[16] and Meyer zu Hörste,[17] on the basis of experimental studies in rats, consider rickets as a phosphorus deficiency disease. The former authors hold that "vitamin D is of importance in the human dietary only in so far as its presence enables the organism to increase the net intestinal absorption of phosphorus from the food."

The conclusion seems warranted, therefore, on the basis of these investigations, that rickets is primarily due to phosphorus deficiency and that lack of vitamin D produces rickets by decreasing the retention of phosphorus, which secondarily depletes the body of calcium.

Vitamin D is seen, then, to serve as an agency for the conservation of the body's calcium and phosphorus stores, acting to maintain the mineral balance. A deficiency of vitamin D leads to calcium and phosphorus depletion, with the inevitable tendency to a fall of calcium and phosphorus in the body fluids. It is this depletion of calcium and phosphorus which is responsible for the subsequent pathologic processes that we recognize as osteomalacia and rickets.

The site of action of vitamin D has not yet been positively established. Inasmuch as only a small proportion of the total phosphorus eliminated from the body is actively excreted into the bowel,[18] it appears more probable, as Telfer,[19] in particular, has maintained, that the beneficial action of vitamin D is to be sought in the increasing of mineral absorption rather than in the decreasing of excretion.

The absorption of calcium and phosphorus is influenced by many factors, in general being enhanced by those which increase the solubility of calcium and phosphate in the intestines and decreased by those which diminish solubility and favor precipitation. Thus, diets very high in phosphate cause calcium depletion by the precipitation of calcium phosphate in the intestine with loss in the feces; high-calcium, low-phosphate diets have a similar effect.[20, 21]

The clinical parallel of the high-phosphate, low-calcium diet is seen in renal rickets, where, owing to the inability of the kidney to excrete phosphate, a shift of excretion of endogenous phosphate to the intestines occurs. To quote Mitchell,[22] "The concentration of phosphorus in the intestine thus increased so blocks the absorption of calcium from the food that the child suffers a true calcium starvation."

Poor utilization of fats and fatty acids also interferes with calcium absorption because fatty acids are left in the intestine to form insoluble calcium soaps.[23] The rickets occurring in celiac disease (steatorrhea, Gee's disease) is ascribed by Shelling and Hopper[24] to the failure of fat absorption with an excess of fat in the stools leading to a loss of calcium as salts of the fatty acids.

A factor held by many to be of considerable importance in rickets is the favorable effect of acids on the absorption of phosphorus[25] and calcium.[21] Thus, the administration of acid[26] and acidifying measures[27] have been shown to bring about limited improvement in rickets by increasing the absorption of calcium and phosphorus.

It has been suggested[27, 28] that vitamin D acts by increasing the acidity of the intestinal contents from allowing freer absorption. Zucker and Matzner[29] found that the intestinal contents in rickets were alkaline and became more acid after the administration of cod-liver oil. This was not confirmed by Redman.[30]

Oser[31] and Shohl and Bing,[32] on the other hand, have in part confirmed Zucker and Matzner's observations. Oser found that the hydrogen ion concentration of the intestinal contents was affected only in the colon. Inasmuch as the small intestines are concerned in the absorption and the colon in the excretion of calcium and phosphate, Oser concluded that rickets is not due to defective calcium absorption but that the primary etiologic disturbance is loss of phosphate from the lower bowel owing to excessive colonic alkalinity. A similar concept was expressed by Bergeim[33] in an earlier publication.

RELATION OF SERUM CALCIUM AND PHOSPHORUS TO PATHOGENESIS OF RICKETS

Depletion of calcium and phosphorus is generally considered to produce rickets by virtue of the serum concentrations being too low to allow calcification to take place. This concept was developed particularly by Howland and Kramer,[3] who postulated an empiric rule, widely adopted clinically, that when the product of the serum calcium and the inorganic phosphate, stated in milligrams per 100 cubic centimeters, is below 30, active rickets is present; when this product is above 40, rickets is either healing or absent. Since this work was done, however, numerous investigations have established the complexity of the state of calcium and phosphorus in the blood, so that the product of the concentrations of calcium and phosphorus cannot be regarded as a simple chemical state conforming to the law of solubility product, and this rather simple view of calcification must seriously be called into question. McGowan[34] has been particularly emphatic in questioning both its chemical and clinical validity.

The state of blood calcium and phosphorus has recently been reviewed comprehensively by Schmidt and Greenberg.[35] Benjamin and Hess[36] recognize at least four forms of calcium and two of phosphorus: (1) an adsorbable calcium-phosphorus complex, constituting about two thirds of the diffusible fraction; (2) a calcium ion constituting the remainder of the diffusible calcium; (3) an adsorbable, nondiffusible calcium-phosphorus complex, constituting about

one fourth of the nondiffusible fraction; and (4) protein-bound calcium constituting the remainder of the nondiffusible fraction.

The manner in which the serum minerals are affected in rickets also indicates that rickets is more than a matter of simple defect in the product of concentrations of calcium and phosphorus. Benjamin and Hess found that the most characteristic change in the serum in rickets was a diminution in the adsorbable calcium-phosphorus complex, which was independent of any change in the total or ultrafiltrable calcium of the serum.

In 1933 Kay and Guyatt[16] found that vitamin D elevates the phosphoric ester content of the blood in the healing of rickets. Stearns and Warweg[37] noted that the organic acid-soluble phosphoric ester in the red blood cells is markedly decreased in active rickets, and that this fraction of the blood phosphorus responds very quickly to vitamin D and may reach the normal value before any definite change in serum inorganic phosphorus is observed. Crimm and Strayer[13b] observed, in 1934, that massive doses of vitamin D increased both the diffusible and nondiffusible fractions of calcium in human blood and that the nondiffusible form was the more affected.

Robison[38] found that rachitic bone calcified in vitro in the complete absence of inorganic phosphate, and with the phosphoric ester of calcium hexose monophosphate, obtained calcification in inorganic solutions over a wide range of calcium and phosphorus concentrations; the minimum level of the product of these concentrations required for calcification was, however, always decidedly lower if the phosphoric ester was present in the solution.

It is thus seen that the concept of the inorganic calcium and phosphorus product as a measure of calcification, while simple, is inadequate. Although blood composition is a limiting factor in calcification and undoubtedly of distinct significance in rickets, as Shipley[4] has remarked, "the process is clearly not one of simple precipitation; it depends on the activity of the living tissue."

Furthermore, it is important to bear in mind that the primary process in rickets, and particularly in osteomalacia, is not defective calcification but decalcification of the shafts of the long bones; Virchow,[39] for that matter, regarded these diseases as a demineralization of calcified bone leaving osteoid tissue. The mechanism of decalcification is, therefore, a basic consideration in the pathogenesis of rickets.

HOMEOSTASIS OF BLOOD CALCIUM: ROLE OF THE PARATHYROID

It is important that serum calcium and phosphorus be maintained at a certain level, not only to allow effective calcification, but to keep a proper concentration of serum calcium, which is necessary for the performance of several other diverse body functions, such as the regulation of muscular excitability and the coagulation of blood. Any appreciable drop in blood calcium results in tetany.

The precise manner by which homeostasis of blood calcium is maintained is, as yet, imperfectly understood. The internal secretions, vitamin D and the intake of calcium and phosphorus all play a part. Aub[40] states, "The parathyroid glands are probably the most important factor in maintaining blood calcium." The skeleton is a reservoir of calcium; the trabeculae of the bones serve as a storehouse for conveniently available calcium, and bone salts are readily withdrawn or deposited according to the body's need (Bauer, Aub and Albright[41]). The chief seat of this calcium storehouse is in the bone trabeculae near the epiphysis (Aub). Evidence that the parathyroid hormone acts on these skeletal reservoirs to maintain blood calcium is abundant—biochemically, histologically and clinically; and the entire subject has recently been surveyed by Collip, Pugsley, Selye and Thomson.[42]

From a normal level of 10 milligrams per 100 cubic centimeters of serum, the calcium falls after parathyroid extirpation to 4 or 5 milligrams. Signs of intense tetany develop in about 20 hours when the blood calcium has fallen below 7 milligrams. When parathormone is injected intramuscularly, there is a latent period of 4 hours after which the blood calcium rises and tetany disappears for approximately 20 hours. The administration of parathormone to the normal individual causes an elevation of serum calcium, and hypercalcemia is a constant feature of hyperparathyroidism.

The evidence is fairly indisputable that the source of this calcium from parathormone action is the bones. The amount of calcium absorbed from the intestines is not influenced by parathormone, and the simultaneous intravenous administration of calcium and parathormone gives merely a summation of their effects, indicating a lack of interaction between them (Thomson and Pugsley[43]). The relation of the parathyroid to vitamin D has been extensively probed, but all evidence indicates that the two mechanisms act independently—both elevating serum calcium, but in different ways. Vitamin D increases retention from the gastrointestinal tract; parathormone increases the amount of calcium liberated into the blood stream from the skeletal reservoir. Thomson and Collip[44] believe that parathormone acts primarily on the bones and causes liberation of calcium by some direct stimulating action. There is histologic evidence to support this view, as the observations of Bodansky and Jaffe,[45] and of Bülbring,[46] suggest active rather than passive liberation of calcium from the bones. Selye,[47] furthermore, demonstrated

that an excess of parathormone increases the production of osteoclasts, which cause disintegration of bone. The decalcification that attends the process is the real cause of the hypercalcemia.

Still further evidence of the decalcifying action of parathormone on the skeleton is found clinically in tumors of the parathyroid which results in the clinical entity of osteitis fibrosa cystica.

ROLE OF THE PARATHYROID IN THE PATHOGENESIS OF RICKETS

The parathyroid glands appear to play a definite role in the pathogenesis of rickets and osteomalacia. Disruption of the calcium-phosphorus balance resulting from vitamin D deficiency stimulates the parathyroid glands to increased functional activity in an attempt to preserve homeostasis of serum calcium by withdrawing calcium from the skeletal reservoir.

Erdheim[48, 49] was the first to note hypertrophy of the parathyroids in osteomalacia (1907) and in rickets (1914). This has been repeatedly corroborated in rickets in human beings (Ritter;[50] Pappenheimer and Minor[51]), in rats (Sekiguchi;[52] Luce[53]), in fowl (Marine;[54] Higgins, Foster and Sheard;[55] Higgins and Sheard;[56] Nonidez and Goodale[57]) and in rabbits (Stoltenberg[58]). Hypertrophy of the parathyroids has also been noted in renal rickets (Langmead and Orr[59]).

Wilder, Higgins and Sheard[60] found in experiments on chicks that "enlargement, hypertrophy and hyperplasia are roughly proportional to the severity of deprivation of vitamin D. Restoring vitamin D to chicks previously deprived of this vitamin and suffering with florid rickets not only causes the rickets to 'heal' but is followed by early regression of the accompanying parathyroid abnormality. The glands not only diminish in size, but the individual cells resume their normal size. The enlargement, hypertrophy and hyperplasia of the parathyroid glands in deficiency of vitamin D is counteracted by subcutaneous injections of parathormone."

Evidence along another line of increased parathyroid activity in rickets is afforded by the demonstration by Hamilton and Schwartz[61] that the serum in rickets has an abnormally high content of parathyroid hormone.

Wilder, Higgins and Sheard believe the conclusion is warranted "that the parathyroid glands are driven to increased functional activity by deficiency of vitamin D." These authors feel that the increased parathyroid activity is a protective mechanism against the development of rickets. There is ample evidence, however, to demonstrate that the opposite conclusion is tenable, namely, overactivity of the parathyroids, far from protecting against the development of rickets, makes the rachitic process worse.

The unfavorable influence of parathormone in rickets has been demonstrated by Waltner[62] in rats, and by Hoag[63] and his associates in children. Fine and Brown[64] found that injections of parathyroid hormone retarded healing in rickets. Shelling, Asher and Jackson[65] reported that in young rats which had been fed rachitogenic diets the daily injection of varying doses of parathormone did not prevent or cure rickets but, on the contrary, intensified the process in the rachitic metaphysis. Collip, Pugsley, Selye and Thomson[42] likewise found that the administration of parathormone exaggerated the rachitic process in rats.

It appears then that parathyroid overactivity, rather than exciting any protective influence against rickets, actually accentuates its development. The possibility suggests itself that this overactivity of the parathyroid, occasioned by vitamin D deficiency in order to maintain serum calcium, forms a direct link in the pathogenesis of rickets.

Experimentally, the administration of parathormone produces bony changes akin to those of rickets. Selye[66] found that "the bony system of young rats is readily and seriously damaged by large doses of parathormone, and the changes so produced are most striking in the region of the epiphyseal junctions in the so-called growth zones. There, the changes are *suggestive of severe rickets* (Selye's italics). . . . Although these changes . . . are suggestive of rickets produced by dietary means, no conclusion as to whether or not the two lesions can be considered identical is possible until further experimental and histologic work now under way is completed."

Shelling, Asher and Jackson[65] found that, when parathormone was given to young rats fed an optimal stock diet, there appeared "evidence of proliferation of the cartilaginous zone so that its number of layers approached that seen in moderate or mild rickets." These authors noted that, "on diets low in phosphorus, parathormone produced proliferation of cartilage as well as stimulation of osteoblastic activity about the trabeculae and endosteum. The calcification, however, was deficient, and the newly formed bone consisted largely of osteoid tissue." These features constitute the typical changes of rickets. In suckling rats, they observed that parathormone produced "cartilage proliferation, delayed ossification of the epiphyseal center, decalcification and replacement of the metaphysis but not typical rickets."

It should not be assumed from these experiments that overactivity of the parathyroids by itself gives rise to rickets. Primary hyperparathyroidism, both clinical and experimental, produces the definite pathologic entity of osteitis fibrosa cystica. The mineral balance in the secondary hyperparathyroidism of rickets is en-

tirely different. In parathyroid adenomas, while there is a moderate reduction of serum phosphorus, the serum calcium is markedly elevated so that conditions are much more favorable for calcification than in rickets, where the blood phosphorus is greatly decreased and the calcium level diminished to a lesser degree. It becomes evident, then, that primary hyperparathyroidism gives rise to osteitis fibrosa cystica. When occurring in consequence of mineral depletion resulting from vitamin D deficiency, in conjunction with defective calcification due to the low serum mineral content, it produces rickets and osteomalacia. The work of Shelling, Asher and Jackson[65] lends support to this view, for these investigators found, as mentioned above, that the bony changes resulting from parathormone administration in young rats varies considerably depending on the diet and that the changes approach those of rickets much more closely in animals fed on a low phosphorus diet than in those maintained on an optimal stock diet.

In line with this hypothesis are the observations of Pappenheimer[67] on parathyroidectomized rats. He found that "a less severe rickets developed in the operated than in the control rats" on a rachitogenic diet. Shelling,[68] remarking on these findings, states: "It is more difficult to produce rickets in parathyroprivic rats than in normal ones, probably because the former would require little or no vitamin D to antagonize the relative hyperfunction of the parathyroids were they intact."

THE PHOSPHATASE MECHANISM IN RICKETS

Still further evidence of parathyroid overactivity as a factor in the pathogenesis of rickets is the similar elevation of bone and serum phosphatase both in hyperparathyroidism and in rickets.

Discovery of the fundamental role of the bone enzyme phosphatase in the past decade has done much to clarify our knowledge regarding calcification. The fundamental investigations of Robison,[38] Kay,[69] and Bodansky and Jaffe[70] may be briefly summarized:

1. "The production of this enzyme (bone phosphatase) forms a part of cellular activity leading to the formation of bone." Phosphatase hydrolyzes phosphoric esters, freeing inorganic phosphate and resulting in a local supersaturation of calcium phosphate, which allows deposition of bone salt.

2. Phosphatase is produced by osteoblasts and is an index of osteoblastic activity.

3. Plasma phosphatase reflects bone phosphatase. Kay explains the high plasma phosphatase in diseases of bone by leakage "at more than the normal rate, possibly because it is produced in excessive amount in the bones in attempted compensation for the lesion."

Pathologically, an increase in serum phosphatase is observed in hyperparathyroidism, Paget's disease, rickets, osteomalacia, carcinoma with osteoplastic metastases to bone[71] and, frequently, in osteogenic sarcoma.[72] Although the prominent lesion in hyperparathyroidism, rickets and osteomalacia is skeletal rarefaction, rather than obvious bone formation, Schmorl[73] has demonstrated histologically in hyperparathyroidism that extensive repair of bone occurs concurrent with destruction; and Albright, Aub and Bauer[71b] have observed a rough correlation between the level of serum phosphatase and the number of osteoblasts in bone biopsies after operation. In rickets, not only is there overproduction of the osteoid matrix, but there is marked proliferation of the cartilage cells, which Robison and Soames[74] have shown to be a fertile source of phosphatase.

The correlation of increased phosphatase activity with these primarily osteoporotic diseases suggests that osteoporosis is a stimulus to regeneration, which is manifest in increased serum phosphatase, which reflects heightened osteoblastic activity in bone.

Thus, one is led to believe that the primary bone lesion in rickets is osteoporosis, and that this condition excites regenerative changes in those portions of the bones capable of osteoblastic activity, and in growing cartilage. In adults, regeneration is restricted, and only the picture of osteomalacia is obtained. It is significant in this regard that the blood phosphatase is but moderately increased in osteomalacia,[70, 75] whereas in rickets very high values may be attained. Children, on the other hand, can respond with active osteoblastic activity and give marked regenerative changes which accentuate the osteoid formation of normal growth. Owing to the disturbance in serum mineral balance, however, calcification is deficient and results in the characteristic clinical features of rickets. The pathologic features are most prominent at the epiphysis because this is the region of most active growth. A further factor in the intensification of the process at the zones of bone growth is the demonstration by Jaffe, Bodansky and Blair[76] that the zones of most active growth are more actively resorbed and that the resorption acts as a further stimulus to osteoblastic activity.

GENERAL METABOLIC DISTURBANCE IN RICKETS

Rickets has thus far been considered as a disease primarily affecting the osseous system, and it is in the bones, to be sure, that the distinctive pathologic changes are found. There are, however, important accompanying features, observed clinically, which very often overshadow the bony deformities and which have received less attention than is deserved. Thus, the rachitic child is often unduly fat, especially in

slight or moderate degrees of rickets.[77] Muscular weakness is almost always present, and the prominent symptoms of potbelly and constipation are usually ascribed to atonic abdominal musculature. The muscles are small, very flabby and poorly developed. The effects of muscular weakness are intensified by laxity of the ligaments.

Although such symptoms as head sweating, anemia, hyperplasia of the lymphoid apparatus, and so forth, are of obscure origin, the disturbance in fat and muscle metabolism may be very reasonably related to the derangement in mineral balance. The calcium of tissues other than bone is normal in amount in rickets,[78, 79] but the phosphorus is low;[80] and so, faulty fat and muscle metabolism is to be attributed to depletion of body phosphorus rather than to calcium deficiency.

The essential role of phosphate ion in the metabolism of carbohydrate is an accepted physiologic fact, and hexosephosphate is an active intermediary in the cellular metabolism. After the administration of glucose or insulin, the inorganic phosphate of the blood and urine falls,[81, 82, 83, 84] while that of the muscles[82] and liver[84] rises, owing to storage of hexosephosphate in these organs. In severe experimental and clinical diabetes where glucose storage in the tissues is impaired, the administration of glucose does not affect the phosphate metabolism.[80, 82] Furthermore, the injection of phosphate has been shown to produce a fall in blood sugar in normal persons and in diabetics.[85]

This intimate metabolic association of glucose and phosphate suggests that the depletion of phosphate in rickets may interfere with carbohydrate metabolism, and evidence has been adduced to indicate that this is indeed the case. Hentschel and Zoeller[86] found that the inorganic and organic phosphate content of the muscles was considerably reduced in rickets and that a return to normal values occurred after administering vitamin D. These authors also reported that in active rickets the ability to synthesize hexosephosphate in the muscles is greatly impaired. Landsberger and Silber[87] regularly found in florid rickets impaired carbohydrate tolerance and a hyperglycemic curve that was not counteracted by insulin. DeToni[88] made similar observations in a certain number of cases. Freudenberg and Welcker[89] also found evidence of disturbed carbohydrate metabolism in rickets.

Phosphate ion plays a fundamental role in muscle metabolism, not only through its association with glucose, but by its combination with creatine, and phosphocreatine is the immediate source of energy in the anaerobic breakdown phase of muscular contraction. Whether this aspect of muscle metabolism is interfered with in rickets, because of phosphate loss, is not yet known.

Fat metabolism is also disturbed in rickets. Niemann[90] and also Landsberger[91] observed that rachitic children are particularly subject to ketosis; and Hottinger[92] found an increase in the excretion of ketone acids in the urine. This may, however, be secondary to impaired carbohydrate tolerance.

A factor hitherto unrecognized in accounting for mineral depletion may warrant brief consideration. Rickets has been considered to be a condition in which primarily there is a decreased phosphorus retention, which acts to carry calcium out of the body; the depletion of calcium sets up the compensatory mechanism of the parathyroids to maintain its level in the blood. Despite the maintenance of a nearly normal level of blood calcium, the serum phosphorus is markedly diminished and has often been considered to parallel the intensity of the disease. It appears that the great diminution in serum phosphorus may not be due solely to its loss through the intestines, but that the depletion may be augmented by increased loss through the urine. In all hyperparathyroid conditions, diminution of serum phosphorus with increased urinary phosphorus excretion is a constant finding. The inability of the kidneys to retain phosphorus in rickets is clearly demonstrated by the phosphate tolerance test of Heymann,[93] in which the blood phosphorus is studied at intervals after the administration of disodium phosphate. Whereas normally a rise in phosphorus occurs, the administration of phosphorus in active rickets fails to increase the inorganic phosphorus of the blood, and the excess phosphorus is promptly excreted in the urine. The manner in which this increased urinary elimination is accomplished is obscure. Perhaps the following mechanism may operate: the kidney, exclusive of the bones, is the organ richest in phosphatase, and an increased phosphatase concentration results in a local hydrolysis of phosphoric esters in the kidney with increased urinary elimination of inorganic phosphate. Whatever the mechanism, the increased urinary phosphorus excretion results in further depletion of the bone-forming minerals.

SUMMARY

Rickets is considered to be a metabolic disease resulting from a disturbance in calcium and phosphorus metabolism. Deficiency of vitamin D results in diminished intestinal retention of phosphorus, which carries out calcium as insoluble calcium phosphate. In an attempt to preserve homeostasis of serum calcium, the parathyroid glands are driven to increased functional activity, releasing calcium from the skeletal reservoirs. The osteoporosis acts as a stimulus to regeneration with increased osteoblastic

activity, especially at the metaphysis of the long bones, where growth is normally greatest and where resorption of bone minerals by parathormone is most active. Owing to disturbed mineral balance, calcification is not wholly successful, and the characteristic features of rickets—abundant osteoid matrix and defective calcification—are produced. The heightened osteoblastic activity is reflected in the serum by increased concentration of phosphatase. The mineral depletion is further accentuated by an increased phosphorus excretion through the kidney—a condition which is encountered in all states of parathyroid hyperactivity, and which is related, possibly, to hydrolysis of organic phosphate by renal phosphatase.

Rickets may be regarded, then, as the consequence of the attempt by the body to preserve a "constant internal environment." It is one of the numerous illustrations of strains on the homeostatic mechanism, where the integrity of one function (blood calcium to protect against tetany) is preserved at the expense of another function (calcification) less immediate to the body's welfare.

In addition to the bony changes, there is a general metabolic disturbance, which is manifest chiefly as muscular weakness. This is due to depletion of body phosphate which interferes with carbohydrate metabolism. It is possible that loss of phosphate may also impair fat and creatine metabolism.

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TWENTY-FIVE YEARS OF UROLOGY*

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AT this, the fiftieth anniversary of the birth of the American Association of Genito-Urinary Surgeons, it seems appropriate to relate what has been accomplished by the Urological Department of the Massachusetts General Hospital since its foundation by Dr. Hugh Cabot in August, 1911, 25 years ago. Dr. Cabot was chief of the department until his resignation in 1920. Since that date, the writer has had the honor of holding this important position.

The figures and tables are presented often without explanation, and always without apology. Some are apparently contradictory, but they must be taken at their face value. The work has been shared by the entire staff, each in his turn, some having more ability and experience than others. It is believed that because of this fact, and because this review covers a long period of time, it represents a very accurate picture of what any similar group of conscientious and well-trained urologists, working harmoniously together, can accomplish. It is probably also true that a similar survey of the work of other clinics that are comparable to ours in size and in the nature of their material, would show about the same results.

This clinic began life with a large and flourishing out patient department, and with 10 beds in the hospital. After a short time it became apparent that more beds were needed, but appeals to this end met with no response until 1929, when we were given 10 more beds; however, even these were not sufficient. This year, as a well-deserved anniversary present, and to satisfy our constant demands, the trustees graciously brought the total number of beds to 25.

For the purposes of this review, all of our 5,263 records have been studied and tabulated. Another member of the staff, Dr. Richard F. O'Neil, has written a very complete history of the various changes in, and developments of, the department. This history will be published elsewhere.

A few general facts are of interest. As will be seen in table 1, the surgical services continued to operate on a considerable number of urological cases until 1924, after which time they withdrew completely from our field. Incidentally, many of these cases had been carefully worked up by our department before the operation was done by the general surgeon. It is also true that during the years up to about 1924, there were on the hospital staff a number of older surgeons who had always done whatever urology came their way, and who, indeed, were quite capable of handling much of it. More recently, most of the younger surgeons find themselves without the training and experience that is now necessary for the practice of urology.

TABLE 1.

Percentage of Urological Cases Operated by General Service

The general operative mortality of our service has naturally varied from year to year, but it has averaged about 4 per cent. The same may be said of our percentage of mistaken diagnoses, which has also hovered just above or just below 4 per cent. Most of the mistakes in diagnosis have involved pathology in the scrotum, a well-recognized source of perplexity and error.

Success in obtaining autopsies has varied from time to time, depending, among other factors, upon the personality and tact of our resident surgeon. In 1 or 2 years it has been as high as 90 per cent, last year it was about 65 per cent. The general average has been about 75 per cent.

Table 2 shows graphically the rapid increase in the number of patients admitted to our service—there were over 100 per cent more in the last five-year period than in the first.*

It has been not only unnecessary but also impossible to do more than touch the "high spots" in this survey. Thus, scrutiny has been directed upon (1) prostatic obstruction; (2) bladder pathology, calculous and neoplastic; (3) kidney pathology, including neoplastic, infectious (both tuberculous and pyogenic), calculous, ptotic and miscellaneous; (4) genital tuberculosis; (5) stricture of the urethra and (6) cancer of the penis.

*In this table, as in tables 8, 9, 10 and 11, the vertical lines indicate 5-year periods.

*Read at the fiftieth annual meeting of the American Association of Genito-Urinary Surgeons, Stockbridge, Mass., May 25, 1936.
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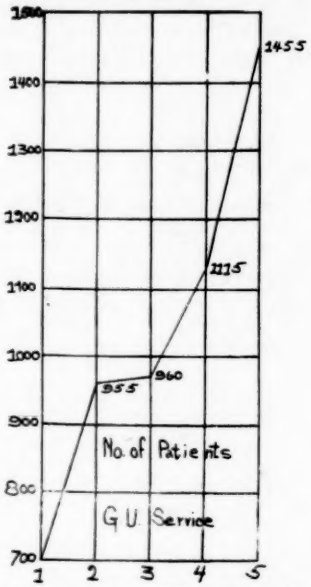
The matter of prostatic obstruction is summarized in tables 3 and 4. There was a total mor-

TABLE 2.



tality of 19.4 per cent. This figure includes both benign and malignant cases, operable and nonoperable. The percentage of malignancy averages lower in this series than it does in certain other series of cases, but at times, in our own experience, it has risen to nearly 25 per cent.

TABLE 3. *Prostatic Obstruction.*

Total = 1124 cases
219 = 19.4% died 199 = 17.7% malignant

No operation or only cystotomy	308	cases with	103	deaths	= 33.4%
Operated all methods	816	" "	116	"	= 14.2%
Benign obstruction	710	" "	94	"	= 13.2%
Malignant "	106	" "	22	"	= 20.7%

One is impressed with a mortality of 33.4 per cent in cases where no operation at all or only a cystoscopy was done. This shows the folly of postponing proper treatment for too long a time. Equally striking is the much greater mortality of the malignant cases throughout. Advocates of the perineal operation may well be

TABLE 4. *Mortality of Type of Operation for Prostatic Obstruction.*

	Perineal	Suprapubic	
		One-stage	Two-stage
1911-1916	18.7%	24.0%	12.4%
1916-1921	20.0%	10.0%	25.5%
1921-1926	8.5%	24.1%	18.1%
1926-1931	5.6%	8.3%	8.9%
1931-1936	8.9%	10.0%	24.2%

cheered by the mortality rate shown as compared with that of the suprapubic operation, whether it be a one- or two-stage procedure. The fact that the average mortality of the two-stage operation is higher than that of the one-stage indicates that those having the two-stage procedure were the poorest risks. All of which review has taught us, at least, that the longer the preoperative drainage, the lower the mortality. Wonder will be expressed at the very few resections that we have done and at the results we obtained, including not only the mortality but also the number of additional operative procedures to which patients undergoing resection were submitted. All we can say is that Boston is a conservative city, slow to take up new ideas. It is also possible that the enthusiastic and, indeed, highly-skilled resectionists who today report mortalities of 1 or 2 per cent, in their first hundred or so cases did no better than we.

The subject of bladder pathology is well covered in table 5. Again as in the prostatic cases,

TABLE 5. *Bladder Pathology.*

NEOPLASM

Total = 351 cases (cancer, 307; papilloma, 44)

Operative mortality	22%
No operation—mortality	20%
Diversion of urinary stream—skin	14 cases
bowel	17 cases
Total cystectomy	15 cases

CALCULUS

Total = 203 cases (66 with benign prostate, 4 with cancer)
Cystotomy—38 cases—mortality, 13%
Litholapaxy—96 cases—mortality, 1.8%
No operation—3 cases—1 died in hospital

one is impressed by the large number of patients who were too poor a risk on admission to have anything more than palliative and supportive treatment. The operative mortality of 22 per cent includes all types of recognized operative procedures, some with and some without the use of radium. Unfortunately, no details were gathered of the cases which had diversion of the urinary stream or which had total cystectomy.

As regards vesical calculus, it is striking to note its great infrequency in the presence of cancer of the prostate. Even more impressive is the tremendous difference in the mortality of litholapaxy as compared with that of cystotomy. Our fondness for litholapaxy may be explained by the fact that this procedure was perfected and given to the profession in 1878 by Dr. Henry J. Bigelow, visiting surgeon to the Massachusetts General Hospital from 1846 to 1886. We of today still use his original technic and, as often as we can get them, his original instruments. The art of crushing a stone in the bladder has been handed on from one generation to another at this hospital. and I hope it always will be. While not without its contraindications and while quite capable of producing harm, we believe that in careful and experienced hands, litholapaxy is the safest and best procedure, and that it should be more widely used. This view is strengthened by the knowledge that residence in the hospital after litholapaxy averages about a week, as compared with about 3 weeks in the event of a cystotomy.

Turning now to kidney pathology, which includes ureteral calculus, the product of our clinic is well shown in tables 6 and 7, in which

TABLE 6. *Renal Disease.*

	All Cases	Operation			No Operation	
		No. Cases	Deaths	Mortality	No. Cases	Deaths
Tuberculosis	296	212	11	5.2%	84	3
Tumor	70	65	9	13.8%	5	1
Stone	439	419	18	4.3%	23	5
Hydronephrosis	46	46	0	0.0	0	0
Pyonephrosis	76	59	10	17.0%	0	0
Nephropexy	69	69	1	1.4%	0	0
Others	70	70	8	11.4%	0	0
Total	1066	940	57	6.0%	112	9 (7.2%)

the facts presented speak for themselves. One or two items deserve mention. In the last two columns in table 6, the large number of patients with tuberculosis who were not operated upon may be accounted for by the statement that they were mostly cases of bilateral involvement. The death which occurred in a case where nephropexy was done took place during the operation, and was undoubtedly due to the anesthetic (gas-oxygen), as at autopsy no demonstrable cause of death could be found. The heading, "Others" in table 6 includes all varieties of kidney pathology not otherwise listed. The portion of table 7 dealing with the kidney and ureter gives more details of the cases of neoplasm and calculus. We are not at all dissatisfied with our results in the operations for calculus, either taken as a whole (5.9 per cent mortality) or where pyelolithotomy was done (2.2 per cent). The term "nephrotomy" in recent years usually means the incision of a single calix or perhaps of one or the other pole of the kidney, as contrasted with the more or less complete bisection of the kidney, which was formerly employed. The results of ureterotomy for stone (2.2 per cent mortality) are quite as gratifying as those of pyelotomy.

TABLE 7. *Kidney, Ureter and Other Operations.*

Organ	Diagnosis	No. Cases	Operation	No.	Deaths	Mortality
Kidney	Tumor	70	Nephrectomy	53	7	13.4%
"	Hydronephrosis	46	"	46	0	0.0%
"	Calculus	439	"	151	9	5.9%
"	"		Pyelotomy	220	5	2.2%
"	"		Nephrotomy	48	4	8.3%
Ureter	Calculus	189	Ureterotomy	189	5	2.2%
Urethra	Stricture		—	237*	15	6.3%
—	Genital Tuberculosis	144	Epi.-vas.	138	0	0.0%
Penis	Carcinoma	47	—	41†	6	14.6%

*21 cystotomies.
†25 groins dissected (8 = 32% malignant).

At this point it may be interesting to glance at tables 8 and 9. In table 8, the sharp drop in the number of operations for renal tuberculosis, in spite of the admission of over 100 per cent more patients, means only one thing—that tuberculosis itself is decreasing and, perhaps, that its earlier recognition and better treatment prevent renal involvement. The rapid rise in the number of cases of ureteral calculus, shown in table 9, may perhaps be accounted for by the better diagnostic facilities now available. More and more use is being made, even by the general surgeon, of the x-ray and of the retrograde or intravenous pyelogram. One must also not forget the ureteral catheter, especially the one that is armed with a wax tip. I think there is no doubt but that, in the not too distant past, many patients with conditions that were diagnosed as appendicitis or some other abdominal

TABLE 8.

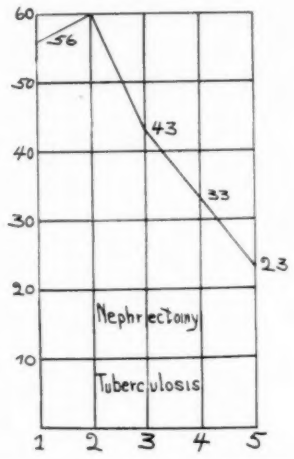
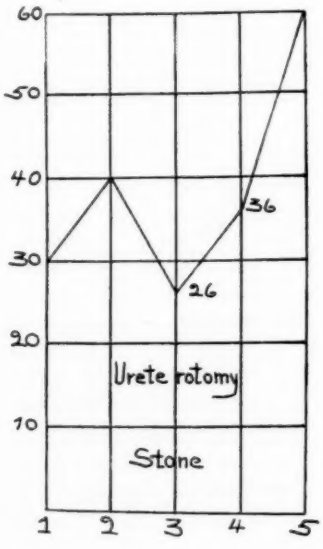


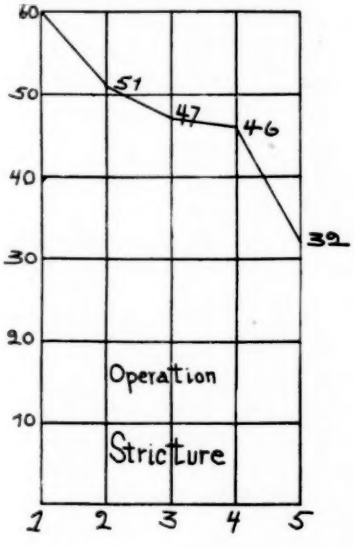
TABLE 9.



condition were, in fact, suffering from ureteral, or possibly from renal, calculus.

Referring again to table 7, one sees that the general mortality in cases of urethral stricture is not excessive. It is noted that in 21 of these cases, cystotomy was done, usually for the improvement of the patient's general condition before the stricture itself was operated upon, but sometimes because retrograde catheterization was necessary. It may be added that in 17 cases of the whole series so-called "extravasation" was recorded, while in 16 the stricture was of traumatic origin. The most interesting and important feature of the stricture group is shown in table 10. Here again, as in the cases

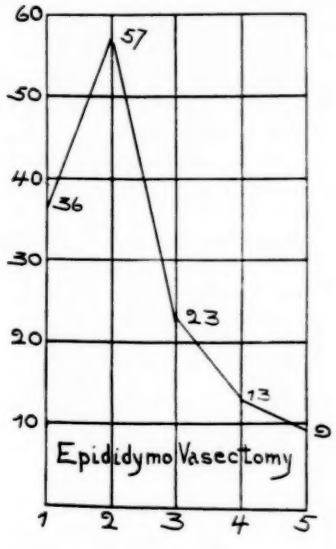
TABLE 10.



of renal tuberculosis, fewer operations were done. In other words, the urologist has found out not only that gradual dilatation is possible in more instances than he formerly thought, but also that the results of this form of treatment are as good or better.

Two more items are now to be considered. In table 7 it is seen that there was no mortality among 138 cases of epididymovasectomy for genital tuberculosis. This is due, I think, to the almost exclusive use of local novocain as an anesthetic instead of general or spinal anesthesia. Many of these patients had bilateral involvement, and a few underwent orchidectomy where it seemed to be indicated. In no instance have we thought it necessary or wise to perform the radical operation advocated by Young, nor have we subjected such patients to any of the so-called palliative and nonsurgical measures. We still believe that epididymovasectomy is the proper procedure, this opinion being substantiated by the good results found in the follow-up of these patients. As in renal tuberculosis, there has been a definite decrease in the number of cases of genital involvement, as shown in table 11. In fact, the curve on this chart and that on table 8 almost parallel one another.

TABLE 11.



Finally, it is of interest to note that where the groins were dissected in cases of penile carcinoma, malignancy was found in the glands in only about one third of the series. The figures are shown in table 7. This corroborates the observations of one of us (J. D. B.) on this disease made many years ago.

In closing this review, we wish to say that it should be noted that these figures apply only to the patients in the open wards of the hospital. It is well recognized that the results in patients such as these are far less satisfactory than in a similar number of private patients. It is regrettable that many rare, interesting and difficult cases could not be included in this brief report. Some of them at least have been, or will be, dealt with in separate communications. Finally, the reader's indulgence is asked if he finds minor discrepancies in the figures presented. We are aware that such discrepancies do exist, but the errors are small and few, and they seemed to be unavoidable in the scrutiny of such a large mass of material.

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*Deceased.

RECENT DEATHS

WETHEY—Francis Van Vechten Wethey, M.D., of Enfield, New Hampshire, died recently at Hanover.

Born at Butte, Montana, in 1893, Dr. Wethey was a graduate of the Hill School at Pottstown, Pennsylvania, and of Dartmouth College. He served in France during the World War and, upon his return from overseas, resumed his medical studies. He was graduated from the University of Vermont College of Medicine in 1924.

He was a member of the New Hampshire Medical Society and the American Medical Association.

His widow, Mrs. Emma Wethey, survives him.

KNOWLTON—John G. W. Knowlton, M.D., a prominent Exeter physician, died at the Exeter Hospital on April 17, after a long illness.

Born in Bath, Maine, February 10, 1874, the son of John and Maria Knowlton, Dr. Knowlton was graduated from Bowdoin College in 1895 and from the Harvard Medical School in 1900. After serving internships at the Boston City and Long Island hospitals he studied in Vienna. Upon his return he practiced in Boston. In 1904 he moved to Exeter, where he resided until his death.

Dr. Knowlton was for a long time a member of the New Hampshire National Guard and organized the 104th Field Hospital. Under his command as major, this unit went to the Mexican border in 1916. The unit was reorganized at the beginning of the World War and, under his command, was sent to France for active duty. Dr. Knowlton was cited for bravery by the English during the battle of Bethune. He was a past commander of the Pingree Post of the American Legion and for many years its historian. He was also a member of the Military Order of the World War and of the Disabled Emergency Officers. He served on the staff of Governor Henry W. Keyes as a military aide. He was a member of the New Hampshire Medical Society, the American Medical Association, the University Club of Boston, and the Masonic Order.

His widow, Mrs. Harriet McCarter Knowlton, and a daughter, Harriet Beatrice, survive him.

RUBLEE—George C. Rublee, M.D., of Rochester, New Hampshire, died recently of a heart attack while on his way home from Florida where he had been spending a vacation. He was in his fifty-fifth year.

A native of Morrisville, Vermont, Dr. Rublee was graduated from the University of Vermont College of Medicine and practiced both at Wolcott and at Hardwick, Vermont. He served in the medical corps during the World War and, on his return from overseas, settled in Rochester. He was a member of the New Hampshire Medical Society and the American Medical Association.

His widow and a daughter, Elizabeth, survive him.

ARE YOU ON A SUCKER LIST?

A man sent $10 to an oil promotion scheme which later failed. Since that time he has received hundreds of letters from promoters of oil wells, mining ventures, aviation promotions and other schemes predicting hundreds of dollars profit from a $10 investment. He is on a "sucker list."

Sucker lists are both born and made, and they represent one of the most valuable capital assets of the underworld. It is not difficult to get your name on a sucker list, but once there, it is almost impossible to get it off.

"Before You Invest—Investigate" is a good slogan to follow if your name is on such a list.—*Boston Better Business Bureau.*

THE YALE CHIMPANZEES

Lessons in thrift are the latest accomplishment of the famous Yale chimpanzees that have already learned to work for "money" discs and to spend them in a "chimpomat," a machine which automatically yields raisins and other chimp tidbits as familiar slot machines give up cigarettes or gum.

Now the chimpanzees have learned to save their pay until a hoard is accumulated and will then carry it from the work room to another room serving as market place where the chimpomat is located and where they can spend their savings.—*Science News Letter*, April 24, 1937.

THE LABORATORY

"A laboratory should be a home in both the proprietory and time-forgetting senses of the word. In the laboratory one must be completely at ease and feel that it is there he belongs. It is not a place to go to work, in the drudgery sense of that word. The laboratory is a place for the joy of learning in which one should always remain a schoolboy with nature as the only true teacher."—Excerpt from an address, "The Spirit of the Laboratory," given by Professor C. R. Stockard at the dedication of the Theobald Smith Memorial Laboratory at Albany Medical College (*Science* **85:344 [Apr. 9] 1937**).

CASE RECORDS
of the
MASSACHUSETTS GENERAL HOSPITAL

ANTEMORTEM AND POSTMORTEM RECORDS AS USED IN WEEKLY CLINICOPATHOLOGICAL EXERCISES

FOUNDED BY RICHARD C. CABOT, M.D.

TRACY B. MALLORY, M.D., *Editor*

CASE 23201

PRESENTATION OF CASE

A 60 year old Norwegian seaman was admitted complaining of abdominal pain.

The patient had been well, except for mild constipation, until 2 years before entry. At that time he began to have difficulty in passing urine and was treated in a Norwegian hospital by catheterization and a series of fourteen x-ray treatments over the lower abdomen. During the succeeding period he had occasional lower abdominal pain during cold weather. This was not accompanied by vomiting. The urinary difficulty cleared up. On the morning of entry he was suddenly seized with severe, cramplike, lower abdominal pain, which recurred every 5 to 15 minutes throughout the day. This was associated with almost continuous bloody diarrhea and repeated vomiting.

Physical examination showed a well-developed and nourished elderly man suffering from severe abdominal pain. The heart was normal, and the lungs were clear. The abdomen was distended, and the flanks bulged. There was tenderness in the lower abdomen, particularly on the right side, and there was also slight spasm in this region. Peristalsis was markedly diminished, and that present was high-pitched and tinkling in character. A rectal examination was negative.

The temperature was 103°F., the pulse 130. The respirations were 40.

The urine showed a specific gravity of 1.022, with a trace of albumin, and the sediment contained an occasional red blood cell and 3 to 5 white blood cells per high-power field. The blood showed a red cell count of 4,500,000, with a hemoglobin of 85 per cent. The white cell count was 13,300, 84 per cent polymorphonuclears. Examination of the stools on one occasion showed a negative reaction and on another a 4+ reaction to the guaiac test. A culture of the stool showed no unusual pathogenic organisms, and no amebae were seen on examination of fresh specimens. The nonprotein nitrogen of the blood was 58 milligrams per cent. A blood Hinton test was negative. The Widal test for agglutinins against *Bacillus typhosus* was negative.

A plain x-ray film of the abdomen showed normal kidney outlines. There were small phleboliths in the region of the right ischial spine, but there were no shadows that were characteristic of calculi. The visualized bones were normal.

The patient's general condition remained unchanged, but the frequency of bloody stools diminished. On the day following entry, marked tenderness in the left lower quadrant and percussion dulness in the right lower quadrant were noted. The temperature remained elevated, and on the third hospital day the vomitus became fecal in character. A laparotomy was performed.

DIFFERENTIAL DIAGNOSIS

DR. LELAND S. MCKITTRICK: I cannot correlate the episode which occurred 2 years before entry with his present illness. He obviously had some difficulty in emptying his bladder. He was catheterized and had x-ray treatments. Whether those were given on the premise that he had carcinoma of the prostate, I do not know.

It seems to me that we have a good deal of evidence that the episode for which he came to the hospital was fairly acute. He was well nourished. He had had a negative history during the 2 years intervening between admissions. He had a red blood cell count of 4,500,000 and a hemoglobin of 85 per cent, and it seems that if he had some chronic illness during that period, the general picture would not be so satisfactory. Therefore, I will take the liberty of thinking that his present entry to the hospital was due to an acute episode not related to anything that we have any evidence of as having gone on in the past. I visualize him as a pretty sick man with an acute onset and with presenting symptoms of lower abdominal cramps. I think that we can assume that they were cramps because the record states that they came at intervals of from 5 to 15 minutes. The outstanding things in addition to the cramps were an almost continuous bloody diarrhea and a physical examination that, in the main, was not very enlightening, except for slight tenderness and spasm in the lower abdomen, particularly on the right side. Peristalsis was diminished. It seems to me that we must draw our conclusions primarily from the story of what has gone on previously rather than from any positive physical findings. Rectal examination was negative. A proctoscopic examination would help a great deal, but is not recorded.

The outstanding facts, as I see them, and the findings that make the most impression on me are three: (1) the sudden, severe, lower abdominal cramps; (2) the story of almost continuous bloody diarrhea, which I think is un-

common; (3) the temperature of 103°F., the pulse of 130 and the respirations of 40 on the day of onset of the disease. It is a rather unusual picture, and I believe that we have the right to assume that the presence of an almost continuous diarrhea means that the patient had pathology which was fairly low in the bowel.

DR. YOUNG: That is overemphasized, Dr. McKittrick. One of the stools was negative.

DR. MCKITTRICK: I am sorry. Then we will start on a different line of attack. I think we have the right to assume that this man had pathology within the abdominal cavity. We also have a right to presume, if he had bloody diarrhea, that he had pathology within the colon. If he had it within the colon, it was one of two things, either a diffuse process, which might give cramps, bloody diarrhea and fever, or a localized process such as a new growth, be it a polyp or be it carcinoma. Assuming a bloody diarrhea and a sudden acute onset, the only way that I can visualize a localized process as causing that picture is by intussusception, with the mass intussuscepting into the bowel below. The intussusception must have been relatively low down with a good deal of squeezing in order to give bleeding and frequent movements, which the record states he had. If one reasons on these lines, it will account for the sudden, severe, localized cramps and for the sudden frequent movements mixed with blood, but it does not satisfactorily answer the sudden sickness of this man, the rapidity with which he became ill, with a temperature of 103°F., a pulse of 130 and respirations of 40 on the day of onset. I do not believe that even an acute intussusception of the large bowel gives that picture very often. If one then approaches it from the point of view of not a definite obstruction but rather an irritative process within the bowel, then one also has to assume that a very acute process has occurred. It seems to me, however, that the frequent bloody movements, the acute onset and the high temperature, pulse and respirations, which point to an acutely ill man, could be much better explained on the premise of some diffuse ulcerating process within the large bowel. I think it is not easy to satisfy oneself with that premise, and of course that is why I said I would have liked to have a proctoscopic examination. It would ease my problems greatly. I have not seen many acute ulcerative processes in the large bowel where pain was such an outstanding symptom so early. Such patients may have a temperature of 103°F., just as this man did, and they may be acutely ill, but as a rule the cramps and the severe pain are not so outstanding. Nevertheless, I have to say something. I believe that he had an ulcerating process within his colon which was diffuse rather than localized. I must content myself with a diagnosis of some form of acute ulcerative colitis; and I think it must extend fairly well down into the rectum.

A PHYSICIAN: Why could he not have a perforation to account for the pain?

DR. MCKITTRICK: The pain is definitely rhythmic, if one can believe the story. It comes with a bang in 5 to 15 minute intervals. He has tenderness in the cecum and over the abdomen, and that is consistent with a diffuse process in the peritoneal cavity. The fact that it was so rhythmic is evidence against perforation.

DR. WILLIAM B. BREED: What about the onset for an acute process?

DR. MCKITTRICK: A patient whom I have followed over a period of years was out rowing, and in the middle of the river he became ill. He had been perfectly all right when he went out. He went to the boat club as fast as he could and when he got to his room he had an acute diarrhea with a temperature of 103°F. Fulminating cases of ulcerative colitis may come on like a bolt out of the blue.

DR. WALTER BAUER: With pain as severe as this? How about the fecal vomiting?

DR. MCKITTRICK: Fecal vomiting occurring so soon in large bowel obstruction is not common. He could have vomiting of the upper intestinal contents, from the peritoneal irritation that goes with the diffuse inflammatory process involving the entire large bowel. I do not want you to think that I am entirely happy with this diagnosis, Dr. Bauer.

CLINICAL DISCUSSION

DR. EDWARD L. YOUNG: This is a patient whom I saw, and I am delighted with Dr. McKittrick's last statement, that he is not happy, because I was not happy at all. The logic of the thing at the time went along in our minds during the 3 days about the same way as it has here. My impression is that the bloody discharge was not so marked as is indicated here. He came in with an acute episode. I was criticized because I did not operate at once. I kept putting off proctoscopy because he was so terribly sick and because there was diarrhea, which we could not control and which would make it somewhat difficult. He was finally scheduled for proctoscopy on this last morning, but the bloody diarrhea increased, his vomiting became definitely fecal, as much as vomiting should ever be allowed to become fecal, and I simply shifted from the proctoscopy to operation. As we discussed it, we thought that an ulcerative process was the best diagnosis. We ruled out intussusception because the cases of acute intussusception that I have seen have not developed such a high temperature and have not run this course. They have shown characteristically longer intervals of freedom from pain and freedom from vomiting, then peristaltic waves have

hit them which started the pain and vomiting again. Moreover, this blood was a great deal brighter than it should have been from intussusception. So I went in, unhappily feeling that I might find an ulcerative process that I could not relieve but still more apprehensive that I might find that I had neglected a malignant obstructing lesion. I did not consider an acute appendicitis.

DR. AUBREY O. HAMPTON: I think it might be worth while to point out that in these x-ray films the gas in the transverse colon is rather pronounced. The colon is moderately dilated and shows an unusual amount of peristalsis. That amount would certainly be against generalized peritonitis. It is also true that there is very little gas on the left side. It is all on the right, and there is no gas in the small bowel.

DR. MCKITTRICK: I meant to ask you about that because there was no note of the gas shadows. If he was distended, the x-ray should show the distribution of gas, and it would help in determining whether it was due to an obstructive process or due to inflammatory disease.

DR. BENJAMIN CASTLEMAN: Will you tell what you found at operation, Dr. Young?

DR. YOUNG: What I found was the most acute, diffuse, necrotic colitis that I have ever happened to go into. The whole large bowel, where we could see it, was tremendously edematous and swollen, and the whole cecum and ascending colon were covered with areas of gangrene, which had not perforated but which were obviously within an hour or two of perforating—a totally hopeless situation. Therefore, there was nothing that we could do to help.

PREOPERATIVE DIAGNOSES

Intestinal obstruction.
Carcinoma of the intestine?

DR. LELAND S. MCKITTRICK'S DIAGNOSIS

Acute diffuse ulcerative colitis.

ANATOMIC DIAGNOSES

Acute idiopathic ulcerative colitis with perforation of the transverse colon.
Peritonitis, acute generalized.
Pulmonary congestion and edema.
Arteriosclerosis, generalized.
Hydrothorax, slight, bilateral.

PATHOLOGICAL DISCUSSION

DR. CASTLEMAN: The autopsy showed a fairly diffuse acute peritonitis with about 150 cubic centimeters of greenish yellow, turbid, peritoneal fluid. In the midportion of the transverse colon was a perforation, about 0.5 centimeters in diameter, which apparently occurred after the operation. The whole bowel, beginning about 3 centimeters above the ileocecal valve and extending all the way to the sigmoid, was purplish red and edematous and was so friable that mere handling produced further perforation. On opening the bowel we found scattered throughout, but especially in the midtransverse colon, large acute ulcers of varying sizes, which penetrated almost to the serosa. We were unable to find any amebae, and are forced to make the diagnosis of acute, nonspecific or idiopathic ulcerative colitis.

A PHYSICIAN: What about the small bowel?

DR. CASTLEMAN: It was slightly distended and edematous but showed no evidence of infection or ulceration.

DR. GEORGE W. HOLMES: Was there anything to explain the treatment that he had in Norway?

DR. CASTLEMAN: At autopsy the prostate was slightly enlarged and weighed 35 grams. Microscopically it showed benign glandular hyperplasia with a slightly more fibrous stroma than usual. The prostate may well have been larger before the x-ray treatment.

CASE 23202

PRESENTATION OF CASE

A 43 year old American housewife was admitted complaining of vomiting and abdominal pain.

The patient had been well until 10 months before coming to the hospital, when she noted that her bowels, which had previously moved daily, failed to move for 2 or 3 days at a time and that she required cathartics about twice a week. On two occasions, however, fresh blood mixed with mucus was noted in the stools. Slight weight loss and fatigability were noted, but there were no symptoms of great significance until 4 months before entry, when she began to have twinges of colicky lower abdominal pain, which occurred five or six times a day and lasted for a minute or two. The pain usually appeared about a half hour after meals but occasioned so little discomfort that the patient paid little attention to it. There was no increase in frequency or intensity of the pain until 3 weeks prior to admission, when it became "quite a nuisance." At this time x-ray studies of the chest, gastrointestinal tract, gall bladder and kidneys were done outside the hospital and showed only "a very active duodenal ulcer with marked gastritis." A restricted diet and powders were prescribed. The colicky pains increased in severity, however, and were occasionally followed by the vomiting of about half a cupful of bile, usually about a half hour after drinking milk. At times there was considerable retching, and the vomitus then contained tiny flecks of blood, but no gross hematemesis occurred. There was no gaseous eructation, py-

rosis or further melena. During the 4 days preceding entry she had almost constant, colicky abdominal pain with no definite localization. These pains were accompanied by uncontrollable vomiting, the character of which was not recorded. Two days before coming to the hospital, an enema produced a fair return but very little gas. On the morning of entry she had a spontaneous bowel movement accompanied by the passage of a small amount of flatus. The stool was normal in appearance.

Physical examination showed a thin, pale woman, who appeared ill but offered no complaints. The lungs were clear. The heart was not enlarged. The heart sounds, however, were poor in quality. The blood pressure was 110/60. The abdomen was resistant on the right side, and there was slight tenderness in that region. A poorly defined mass was palpable in the right side of the abdomen at the level of the umbilicus. The mass did not move with respiration, and pressure over it produced pain on the left side. Rectal examination was negative, and the ampulla was filled with soft, brownish green feces. A vaginal examination was noncontributory.

The temperature, pulse and respirations were normal.

Examination of the urine showed a specific gravity of 1.034, with a trace of albumin. A test with Benedict's reagent showed an orange precipitate, and the examination for the presence of diacetic acid and acetone was positive. The sediment contained 10 red blood cells and 3 white blood cells per high power field and many epithelial cells. It was not a catheter specimen. The blood showed a red cell count of 3,500,000, with a hemoglobin of 65 per cent. The white cells numbered 7,900. A stool specimen gave a 3+ reaction to the guaiac test. The blood sugar was 78 milligrams per cent, and the nonprotein nitrogen was 27 milligrams per cent. The blood chlorides were equivalent to 104 cubic centimeters of N/10 sodium chloride per 100 cubic centimeters.

A plain film of the abdomen showed both kidney outlines to be normal in size and position. The gas shadows present in the abdomen were scattered along the sigmoid and along the left side of the small intestine. There was no gas in the right side, but there was an increase in density in the soft tissues simulating a distended cecum. There was also an indefinite, rounded, soft tissue shadow extending downward from the region of the liver edge. The liver edge, however, was not demonstrable.

On the third hospital day a laparotomy was performed.

Differential Diagnosis

Dr. Marshall K. Bartlett: In the first place, this is quite a long story. It goes back 10 months, at which time this woman had a very definite change in bowel habits. That is all she noticed until 4 months before entry, when she began to have colicky lower abdominal pain which occurred several times a day but which lasted only a very short time and apparently did not bother her very much. During this time she noted fresh blood and mucus with bowel movements on two occasions. About 3 weeks before entry, the pain became much worse, and she had x-rays taken, which showed a very active duodenal ulcer. I do not know what to make of that. The story up to that point would not have made me think of duodenal ulcer in any way. I think we are apt to take too lightly x-rays that are taken outside of our own hospital by people whom we do not know. Of course, this is a dangerous thing to do, but I am inclined to believe that a duodenal ulcer, if present, was not the cause of her present symptoms. Her diet gave no relief, and she began to vomit occasionally. She drank some milk and a half hour later vomited half a cupful of bile. That looks to me as though the stomach were emptying rapidly and the milk had all passed out of it. The tiny flecks of blood can be explained on a mechanical basis. I doubt if she had a bleeding lesion in the stomach. For 4 days she had almost constant, colicky pain with no definite localization. That is the type of pain we associate with increased and abnormal, small bowel activity, and with this she had a good deal of uncontrollable vomiting. During the 2 days before she came in she had two bowel movements, one with an enema and one without. It is a long story of gradually increasing, colicky abdominal pain without localization, which started very mildly 4 months before entry and became steadily worse until she came in.

On physical examination a poorly defined mass in the right side of the abdomen at the level of the umbilicus was found. It did not move with respiration, and pressure on it produced pain on the left side. It is interesting to me that this woman with all that colicky pain was not distended. I generally associate an obstructive lesion with colicky pain, and with such a long duration of pain one would expect to have some signs of distention. It is interesting that pressure on the mass referred pain to the left side.

The laboratory report does not help me very much. I am inclined to explain the urinary findings on the basis of dehydration as a result of vomiting. She had a moderate anemia. The white cell count was normal. The stool showed a 3+ guaiac reaction, and the chemistry was normal, except that the chlorides were a shade high. If she had been vomiting, I would have expected the chlorides to be lower, but possibly she had been given some parenteral fluid and salt.

X-ray Interpretation

Dr. George W. Holmes: This film was described in the record, and I can add very little to what was said there. I might point out the things that were mentioned. You can see the outline of the left kidney fairly well. Here is a shadow on the right, which may be the kidney. This looks to me like the liver edge. We have a shadow here which looks like the gall bladder. It is not particularly large or abnormal in shape, and I would interpret it as a normal gall bladder. There is no evidence of free gas or distention of any part of the gastrointestinal tract. This gas that you see scattered along the left side, particularly in the pelvis, looks like gas in the terminal ileum. While that is not a normal finding, it is still not particularly uncommon in people with abdominal pain. You would expect to see more gas in the cecum and transverse colon in a normal subject.

Differential Diagnosis Continued

Dr. Bartlett: We will start with the most common lesion in the right side of the abdomen. Was this due to appendicitis? I am inclined to think that it was not. In a woman of her age one should be able to make out a story of acute onset of some kind. If it was an appendiceal abscess, it was a good-sized one. The temperature was normal, the white blood cell count was only 7,900. Also, an appendiceal abscess ordinarily would not explain the positive guaiac reaction and the blood in the stools. The type of pain that she had does not fit appendicitis, and I am inclined to rule out that diagnosis. Of course, with the x-ray finding of a very acute duodenal ulcer, one cannot help thinking of the possibility of perforation. There again, nothing in the story is suggestive. There was no acute episode dating far enough back to give a pocket in the right side. I think the same arguments that are against appendicitis are also against perforation of an ulcer. Is this a lesion of the gall bladder? The abdominal mass did not move with respiration, and the story and the type of pain do not fit. I am inclined to rule out the kidney on the basis of the normal kidney shadow on the flat plate and to rule out a pelvic tumor on the basis of the vaginal examination.

Is it a malignant lesion in the cecum? If so, it is a big one, and her pain must be due to obstruction; she was not distended, and the x-rays did not show dilated loops of bowel. I would think that she would have more bleeding from a mass of this size in the colon, for, although she bled some, she did not bleed a great deal. Malignant tumor probably is statistically the best bet, but it does not entirely fit the picture.

The only thing that does fit is intussusception. Of course, that is rare in adults, but on the other hand it does explain all the symptoms. Her pain is of the small bowel type, I should say. Pressure on the mass gave her pain on the left side, probably because of traction of the mesentery of the small bowel. She bled a little and had blood and mucus on two occasions. It seems to me that intussusception fits this story better than anything else. The distended cecum with no gas in it can be explained on this basis. My experience with intussusception in adults is not extensive. I believe that it is very commonly produced by a tumor of the small bowel. I should not be surprised if she has intussusception due to a benign tumor of the small bowel, and that is my diagnosis.

Dr. Tracy B. Mallory: Are there any other suggestions?

Dr. J. H. Means: Is regional ileitis to be considered?

Dr. Bartlett: Yes, I think it has to be considered, but I cannot prove it one way or the other.

A Physician: It strikes me as surprising that vomiting has been such a marked feature and that distention of the abdomen was not a marked finding. Would you expect to find a lesion any higher, in the upper intestinal region?

Dr. Bartlett: The mass was on the right side. She had a great deal of pain and vomiting, but no distention.

Preoperative Diagnosis

Carcinoma of the cecum.

Dr. Marshall K. Bartlett's Diagnoses

Intussusception.
Benign tumor of the small bowel?

Anatomic Diagnosis

Adenocarcinoma of the cecum, grade II.

Pathological Discussion

Dr. Mallory: I think that Dr. Bartlett has convinced all of us that this patient was suffering from intermittent intestinal obstruction and that obstruction was probably in the small intestine. What we found was a carcinoma in the cecum, but I think Dr. Bartlett was perfectly correct in his interpretation of the symptomatology because this carcinoma, as you can see, is a polypoid tumor, and it arises immediately beneath the margin of the ileocecal valve. With a tumor in this location, there are theoretically two possible ways in which intermittent obstruction can occur. Within a few months we have presented a similar case—a carcinoma at the ileocecal valve with intermittent obstruction. In that case the roentgenologist was able to demonstrate intussusception of the terminal ileum into the cecum, and since the patient was oper-

ated on during a period of obstruction, this was confirmed surgically. Apparently involvement of the valve may in some way predispose to invagination of the ileum into the cecum. Another possibility, however, especially where the tumor is mobile and not too large, as in the present case, is that the tumor might invaginate into the terminal ileum. This would necessitate reverse peristalsis but does not seem to me inconceivable. I wonder if the roentgenologists in retrospect can give us any further information.

DR. HOLMES: Perhaps we should have laid more stress on the gas-filled ileum and on the complete absence of gas in the ascending colon. What do you think about it, Dr. Schatzki?

DR. RICHARD SCHATZKI: I doubt if one would ever suspect pathology in the cecum from examination of this film without knowledge of the clinical findings. However, when one looks at it again, in view of our present information, it is evident that there is a cylindrical soft-tissue mass, which does not have the pattern of fecal material, in the region of the ascending colon. It would be perfectly explained by intussusception of the terminal ileum into the colon, and I believe the x-ray evidence strongly suggests that this did occur.

DR. MEANS: What about the ulcer?

DR. MALLORY: We cannot tell you about that, unfortunately. This tumor was resected, and the patient made a satisfactory recovery.

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PRESIDENTIAL MESSAGE CONCERNING THE ANNUAL MEETING

THE one hundred and fifty-sixth annual meeting of the Massachusetts Medical Society will take place in Boston June 1, 2 and 3 at the Hotel Bradford. I consider the meeting one of the most important that the Society has ever held. Not only is this true from a scientific aspect but also from the standpoint of the position that organized medicine may occupy in relation to society, in its broadest aspect.

The very efficient Committee of Arrangements, under the leadership of Dr. Horatio Rogers, has worked assiduously since September, 1936. The attractive program which it will present is comprehensive in scope and meticulous in detail. They have striven to appeal to the demands of all practitioners of medicine. The doctor who has practiced for thirty-five or forty years will find sufficient to allow him to indulge in retrospect to his heart's content. He himself was a participant in the wonderful change that has come over the practice of medicine. His contribution to the success of the change was gratuitously given. His judicious assistance was a valuable factor in the development of modern medicine.

The younger practitioner, as he studies the program, will find that all the past in medicine belongs to him and is entrusted to his care. He will find no sign of the narrowing of opportunities in the field of professional medical activity. On the contrary he will see a greater scope for the practice of his art in the future than was ever offered to the practitioner of the past. There need be no boundary to his scientific ambition, provided his scientific sense is accompanied by some imagination. For all true scientists have some imagination.

The innovation of a clinical meeting will certainly be a convenience, and, it is hoped, will also prove a conservator of time. Moreover, as this is an experiment in our program, I would call for a large attendance in order that we can determine whether the profession approves of the innovation. As usual the subject matters that will be discussed at the Sections have been well chosen and are of practical importance to the rank and file of the Society. The Section officers have tried to include in their programs matter that will be of the greatest interest to the greatest number. The entertainment provided for the ladies is especially attractive.

The principal address at the annual dinner will be given by Charles Gordon Heyd, M.D., president of the American Medical Association. As it is the first time that the president of the American Medical Association has spoken formally at our annual meeting, I trust that there will be a large attendance.

The Annual Meeting gives an opportunity to the profession to renew old acquaintances, to form new ones, to discuss scientific subjects, to talk over the trends in medical practice as they see them, and to contribute much good based upon their experience over the years in taking care of the sick. The Sections will give the widest opportunity for every member to discuss the subject matter presented at their respective meetings.

The executive officers urge every member to

attend this important annual meeting. For after all is said and done, it is the rank and file of the profession who make public medical opinion.

CHARLES E. MONGAN.

ONE MILLION VOLT X-RAYS

THE amount of radiation that can be delivered to a deep-seated neoplasm by means of x-ray is dependent upon four factors: the voltage at which the x-rays are produced; the character and thickness of the filter material; the distance of the source of radiation from the patient; the tolerance of the superficial tissues. By increasing the voltage the x-ray beam acquires shorter and more penetrating wave lengths. The undesirable longer wave lengths are removed by interposing filters of aluminum, copper, tin or lead between the source of radiation and the patient. Since the inverse square law of distance applies to the intensity of x-rays as it does to light rays, it is important that the source of radiation be at some distance from the patient when a deep-seated new-growth is irradiated. It is a well established fact that the normal skin has a greater tolerance for the shorter, more penetrating rays than for the longer wave lengths. Thus, to obtain a large-depth dose one employs a high voltage, a heavy filter and a long distance. Conversely, a small-depth dose results from low voltage, light filtration and short distance.

About 15 years ago an x-ray therapy unit operating at almost 200,000 volts was installed at the Collis P. Huntington Memorial Hospital by the late Dr. William Duane. This was the only machine of its kind in New England. Shortly after this a similar unit was put into operation at the Massachusetts General Hospital. For a number of years these machines were regarded with great skepticism by many members of the medical profession. Today the radiation treatment of malignant disease, whether in a hospital clinic or in the private office of a physician, is carried out largely by this type of apparatus. There are at least two dozen such units within a 40 mile radius of Boston. It has taken 15 years for the 200,000 volt x-ray therapy unit to prove its worth.

It has become apparent to many radiologists that wave lengths shorter than those obtained at 200,000 volts are highly desirable in the treatment of malignancy. This has led to the use of increased filtration, and the operation of 200,000 volt x-ray tubes beyond their rated capacity. Although such practice increases the penetrating power of the x-ray beam only to a slight degree, the improved therapeutic results have justified the decrease in economy of operation.

The external application of radium in the treatment of the inaccessible deep-seated malignancies has been possible in only a few large clinics. Even though several grams of the element are available, the intensity of radiation is so small that the distance between the patient and the applicator cannot be made sufficiently great to deliver with economy an adequate depth dose. It is, however, the opinion of many that if radium were obtainable in sufficient quantities it would offer the ideal means of external radiation.

The only difference between x-rays produced at 200,000 volts and the gamma rays of radium is in their wave lengths. If the voltage at which x-rays are produced could be made sufficiently high, then x-rays and radium rays would become identical. For a number of years physicists and engineers have been working on the problem of providing a source of very high voltage x-rays that would approximate in wave length the gamma rays of radium, and that could be produced in intensities equalling the output of several hundred grams of radium element. These endeavors have been rewarded with varying degrees of success.

Shortly after the discovery of x-rays by Roentgen, their value in the field of medicine, particularly as a diagnostic agent, was recognized, and various types of apparatus were devised for their production. Most of these machines were of the "electrostatic" type and produced fairly high voltages with small currents. These electrostatic machines were erratic in their performance and were eventually replaced by the more stable electromagnetic generators, which develop higher currents at lower voltages.

A research group at the Massachusetts Institute of Technology, working on nuclear disintegration, recently developed an electrostatic generator capable of producing 5,000,000 volts. It appeared to be a step backward when it was suggested that a generator of this type, operating at about 1,000,000 volts, be used for the

production of x-rays for therapeutic purposes. On investigation, however, it became apparent that considerable ingenuity and modern engineering had transformed the electrostatic generator into a machine of great reliability of operation and comparative simplicity of construction.

Through the generosity of the Godfrey M. Hyams Trust, the construction and installation of such a machine has been made possible at the Collis P. Huntington Memorial Hospital. A description of this apparatus was presented at the annual meeting of the American Roentgen Ray Society and is now in press. During several months' operation, the machine has proved as reliable as one of the commercial 200,000 volt units. The control is simple, and anyone familiar with x-ray apparatus can learn to operate the unit in a few minutes. The machine is being run at a constant potential of 1,200,000 volts, which is the highest effective voltage ever used for the production of therapeutic x-rays. The output of radiation is so great that it has been found necessary to run the apparatus at less than one half of its rated current capacity.

The average daily treatment of 300 r., using a distance of 70 centimeters and a filter equivalent to 6 millimeters of lead, is given in 5 minutes. This treatment time could be cut to 2 minutes if desired. The penetrating power is so great that it takes 10.5 millimeters additional copper filtration to decrease the x-ray intensity to one half its strength. By comparison, only 1.2 millimeters of copper is required to produce the same result with 200,000 volt x-rays. The skin tolerance for 1,000,000 volt x-rays is double that of 200,000 volt x-rays, which fact, combined with the greater penetrating power, allows the administration of very large doses without the danger of untoward superficial reaction.

From the standpoint of the radiotherapist, all cases of malignant disease may be divided into three groups. In the first are those cases presenting tumors which are known to be radioresistant and in which radiation can be expected to be of very little value. The second consists of those cases in which the growth is so extensive that there is no hope for cure by any method of treatment. In these cases considerable palliation may be secured, such as relief of pain, arrest of hemorrhage and healing of ulceration, by moderate radiation. Large doses frequently make such patients systemically worse. In the third are those cases presenting tumors which are known to be radiosensitive, and in which the disease is not too extensive. It is in the latter group that we may expect improved results from very high voltage x-rays, particularly when the lesions are deep-seated. It remains for time and experience to tell us how much advancement can be made.

THIS WEEK'S ISSUE

CONTAINS articles by the following named authors:

LINTON, ROBERT R. M.D. Harvard Medical School, 1925. F.A.C.S. Instructor in surgery, Harvard Medical School. Assistant surgeon, Massachusetts General Hospital. Address: Massachusetts General Hospital, Boston. His subject is "Acute Peripheral Arterial Occlusion and Its Treatment." Page 871.

GUBNER, RICHARD. M.D. New York University College of Medicine, 1936. Intern, Kings County Hospital, Brooklyn, N. Y. Address: 1554 Ocean Avenue, Brooklyn, N. Y. His subject is "The Metabolic Background of Rickets An Interpretive Review." Page 879.

BARNEY, J. DELLINGER. M.D. Harvard Medical School, 1904. F.A.C.S. Chief-of-service, Urological Department, Massachusetts General Hospital. Assistant professor, genito-urinary surgery, Harvard Medical School. Address: 87 Marlboro Street, Boston.

MINTZ, E. ROSS. M.D. Université de Paris, Faculté de Médecine, 1928. Assistant urologist, Massachusetts General Hospital. Assistant in genito-urinary surgery, Harvard Medical School. Address: 6 Commonwealth Avenue, Boston. Their subject is "Twenty-Five Years of Urology." Page 888.

The Massachusetts Medical Society

ANNUAL MEETING OF THE COUNCIL

THE annual meeting of the Council will be held in the Penthouse of the Hotel Bradford, Boston, on Wednesday, June 2, 1937, at 10:30 o'clock.

Business:

1. Reading record of last meeting in abstract.
2. Nominating Committee retire to deliberate.
3. Report of Committee on Membership and Finance.

4. Reports of Committees to consider petitions for restoration to the privileges of fellowship and new committees to be appointed.
5. Reports of Standing Committees and Special Committees.
6. Election of Officers and Orator by ballot.
7. Appointment of Committees for ensuing year, both Standing and Special.
8. Proposed changes in By-Laws.
9. Incidental business.

ALEXANDER S. BEGG, M.D.,
Secretary.

Boston, May 25, 1937.

Councilors are asked to sign one of the two attendance books before the meeting.

The Cotting Luncheon will be served immediately after the meeting.

SECTION OF OBSTETRICS AND GYNECOLOGY*

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1101 Beacon St.,
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CASE HISTORIES

No. 20. COMBINED EXTRA-UTERINE AND INTRA-UTERINE PREGNANCY

Mrs. J., a white woman, aged 24, was seen in consultation August 22. Her last regular period had occurred June 12. On July 23 the patient began to flow and developed sharp pains in the right lower quadrant. Her family doctor performed a curettage at home on August 7. The flowing and pains continued intermittently and were accompanied by dizziness and syncope. The patient also complained of a dull, constant pain in the lower abdomen, which was aggravated by sitting up or by attempts at defecation.

There was no family history of tuberculosis, diabetes, malignancy or hemorrhagic disease. Except for childhood illnesses her health had always been excellent. There had been no previous pregnancies. The menses had started at the age of 11 and had been regular and normal in amount, but they were rather painful the first day. There had been no discharge between the periods and no symptoms of pelvic inflammation.

Physical examination revealed a well-nourished young woman with marked pallor of the skin and mucous membranes and a temperature of 98.2°F. There was a tender abdominal mass, which was more prominent on the right and which extended to the level of the umbilicus. Vaginal examination showed a nulliparous introitus with a slight bloody show. The cervix was closed, and movement of it caused intense pain. The fundus seemed displaced to the left but could not be definitely outlined. The patient was transferred to St. Margaret's Hospital, Dorchester, with a diagnosis of ruptured extra-uterine pregnancy.

On August 23, under gas-ether anesthesia, the abdomen was opened by a median suprapubic incision, exposing a hematocele, which filled the right side of the pelvis. The clots and fluid blood were removed, disclosing a rupture of the outer third of the right tube. The uterus, right ovary and left adnexa appeared normal. After a right salpingectomy had been performed, the abdomen was closed without drainage. Recovery was uneventful.

Seventeen months later the patient was delivered, by low forceps, of a normal, full-term baby.

Eight months postpartum, after missing two periods, she began to flow and developed severe pain in the lower left quadrant. She said, "I think my left tube is bursting!"

Examination disclosed a moderate, bright red flow, a closed cervix and the uterus enlarged to the size of a 10 weeks' pregnancy, with the fundus in good anterior position. There was general pelvic tenderness. This was most marked in the left vault which contained a doughy, tender mass. The patient was transferred to the Carney Hospital and was prepared for immediate operation.

The blood pressure was 104 systolic, 74 diastolic, and the pulse rate was 104 per minute. Donors were secured for a possible blood transfusion, but this proved to be unnecessary.

The abdomen was reopened in the median line, and a large amount of free blood and clots were found. There was a break in the middle third of the left tube, which contained a ruptured vessel pumping blood. The uterus appeared larger than usual for a tubal pregnancy. A left salpingectomy was done, the blood clots were removed, but most of the fluid blood was undisturbed. The incision was closed without drainage. As an intra-uterine pregnancy was suspected, the patient was kept under the influence of morphine for 3 days, and, on the fourth day after operation, she expelled a 2 months' fetus with the membranes intact. She made a good recovery and was discharged on the fourteenth day.

Comment. Coexisting extra-uterine and intra-uterine pregnancy is not extremely rare. About 300 cases have been reported. Clinically, the condition should be borne in mind, lest the passage of a fetus by vagina lull one into a false sense of security concerning extra-uterine pregnancy.

*A series of selected case histories by members of the Section will be published weekly.

Comments and questions by subscribers are solicited and will be discussed by members of the Section.

MISCELLANY

BOSTON TUBERCULOSIS ASSOCIATION HEAD ADDRESSES DISTRICT SOCIETIES

Dr. John B. Hawes, 2nd, president of the Boston Tuberculosis Association, spoke before the Franklin County District Medical Society on "Dust and Its Effect on the Lungs" at its last meeting. He also addressed the Berkshire Medical Society at Pittsfield on May 13 on the subject, "The Relation of Industrial Dusts to Disease."

AMERICAN ASSOCIATION OF PHYSICIANS

At the annual meeting of the American Association of Physicians, recently held in Atlantic City, Dr. George R. Minot, of Boston, was elected president for the coming year. He succeeds Dr. Thomas R. Boggs, of Baltimore.

DR. RIVERS TO SUCCEED DR. COLE AS DIRECTOR OF THE ROCKEFELLER HOSPITAL

The Board of Scientific Directors of The Rockefeller Institute for Medical Research recently announced that Dr. Thomas Milton Rivers, at present a member of the Rockefeller Institute, had been selected as director of the Department of the Hospital of the Institute to succeed Dr. Rufus Cole, who has reached the age of retirement and is withdrawing from the directorship of the hospital on June 30, the end of this academic year.

NATIONAL HEALTH CONTEST

Names of cities and counties in the United States that do most to protect the health of their inhabitants have just been announced. These are the winners this year in the city and rural health conservation contests conducted annually by the Chamber of Commerce of the United States with the American Public Health Association.

Milwaukee, Wis., is winner among competing cities of over 500,000 population. Reward for meritorious achievement was given to Pittsburgh. Other winners are: for cities between 250,000 and 500,000, Dallas, Texas; for cities between 100,000 and 250,000, New Haven, Conn.; for cities between 50,000 and 100,000, Pasadena, Calif.; for cities between 20,000 and 50,000, Greenwich, Conn.; for cities under 20,000, Middletown, N. Y.

In the rural contest the country is divided into six geographic areas. Winners of this contest are: for the northeastern division, Columbia Co., N. Y.; for the eastern division, Davidson Co., Tenn.; for the southeastern division, Pike Co., Miss.; for the north central division, Shawnee Co., Kans.; for the south central division, Dallas Co., Texas; for the western division, Los Angeles, Calif.

Not all cities in the country compete. Improvement in health and a saving of thousands of lives, however, are believed to have been accomplished as a result of the stimulation to health protection which participation in the contest provides. Among the larger cities, for example, the 26 cities which have continuously competed had in 1934, the last year for which complete returns are available, a death rate which if it had prevailed in the remaining large cities of the country would have represented a saving of 19,600 lives annually.—*Science News Letter*, April 24, 1937.

CORRESPONDENCE

LABORATORY TECHNICIANS

May 12, 1937.

Editor, *New England Journal of Medicine*,

The importance of the laboratory as an aid to the clinician in making diagnoses has increased rapidly during the last few years and will continue to assume even greater importance in the future. The advancements in the fields of chemistry, physics and biology have given us new laboratory aids that call for more training and ability in laboratory workers than has ever been the case before. Are we keeping pace in the training of personnel for laboratory positions with the new demands that are being put upon them?

A very important step in advance in contributing to standards for technologists has been made by the American Society of Clinical Pathologists, which recently established a registry for qualified persons and set up minimum standards for schools offering training for such persons. In their most recent roster they list 109 schools that meet the minimum requirements of their Board of Registry and also list over 3,000 men and women who qualify for this profession under their regulations. While the writer does not approve of all the details that are set up by this Society for approved schools, he firmly believes in the general principle involved and recognizes that persons who successfully complete the curriculum described by this Society have a superior training, as compared with many still engaging in the profession of hospital laboratory technician.

During the years of the depression there was unquestionably a deterioration in the standards that were set by many hospitals for the employment of technicians. This was largely due to the incentive to economize by taking in unpaid apprentices who, it was believed, would be of some use in routine matters while they were acquiring some "rule of thumb" skill in the simpler laboratory procedures. That many excellent technicians have been trained in this way cannot be doubted, but it does not follow that just because a high school graduate, or even a college graduate, wants to be a technician that she can be made into one by this kind of apprenticeship, regardless of her previous scientific training.

With the increasing field of employment, many schools have grown up which are highly commercialized, and many courses have been developed in connection with hospitals that are calculated to combine service and training as described above. We

now find that junior colleges are rapidly entering this field of technical training, offering in increasing numbers courses in laboratory procedures during their last year. There are, undoubtedly, positions of a character which can be successfully filled by such superficially trained persons who have no knowledge of the fundamental scientific principles underlying the procedures. Those who employ technicians should carefully differentiate such routine test tube analysts and those who may be vested with larger responsibilities, who may be expected to advance professionally, or who may be of value in perfecting methods or assisting in research.

The duties and responsibilities that devolve upon hospital laboratory technicians are of a serious nature and call for character and judgment, as well as technical skill. Many physicians look upon the laboratory as giving infallible evidence, as compared with the symptoms that may be observed at the bedside. There are, of course, borderline results in laboratory specimens, as well as borderline symptoms, which must be interpreted with caution. Laboratory results may determine the life or death of the patient, may indicate the need for a serious and expensive operation, or may relieve the anxiety of the patient that such is necessary. For these and many other reasons, we believe that persons selected by a rigorous educational process, well-trained in the sciences, including theory, with a final technical training imposed upon the fundamental background, is not expecting too much. Character cannot be made by education, and people who obviously lack character and poise should be discouraged from going into this profession.

It is chiefly in the hands of clinical pathologists to raise the standards of this profession to the scientific level and dignity that it deserves. However, to a lesser extent, hospital staffs and practicing physicians can, and should, give this matter serious consideration and demand that the routine services in the hospital laboratories should be performed only by skilled, trained, conscientious, reliable persons. This matter is of growing concern as the variety and complexity of the tests performed in hospital laboratories increase with the advancement of the sciences.

Very truly yours,
C. M. HILLIARD,
Professor of Biology and Health.

Simmons College,
Laboratory of Biology and Health,
Boston.

MINIMIZING PAIN IN THEELIN INJECTIONS

May 7, 1937.

Editor, *New England Journal of Medicine,*

In the theelin treatment of gonorrheal vaginitis in children the pain of the daily injection is a considerable drawback to this type of treatment. Bearing in mind the chemical compatibility of theelin with novocain and adrenalin I found that infiltration of the injected area with 1 cc. of novocain in 1:1/10,000 adrenaline chloride resulted in a painless injection, avoiding considerable psychic trauma to the child. In treating one child for a relapse, the cornified epithelial cells and the disappearance of pus occurred at approximately the same period as in the original treatment without the novocain. Later I found that the novocain and aqueous theelin could be mixed in the syringe and, if injected very slowly, gave as painless an injection, without demonstrable loss of efficiency. In view of the fear of painful injections that prohibits the use of aqueous theelin in many adults, I feel this suggestion worth passing along.

Very truly yours,
ROBERT B. BARTON, M.D.

162 Washington Street,
Wellesley Hills,
Massachusetts.

RECENT DEATH

BOYD—SAMUEL GEORGE BOYD, M.D., of 1960 Hyde Street, San Francisco, California, died January 2.

Born in 1861, Dr. Boyd was graduated from the Harvard Medical School in 1885. He was a nonresident member of the Massachusetts Medical Society.

OBITUARY

RESOLUTION ON THE DEATH OF DOCTOR DANIEL P. O'BRIEN

Whereas, our friend and associate Doctor Daniel P. O'Brien has been removed by death from our midst, and whereas, we the Staff of Saint Luke's Hospital of New Bedford, Massachusetts, keenly feeling our loss, wish to register our appreciation of his kindly qualities, his helping hand to his associates and his patients, his steadfast loyalty to this hospital, the community and our country, and to tender our sympathy to his family, it is moved and unanimously ordered that this resolution be spread upon our records and, further, that copies thereof be sent to his widow and to the *New England Journal of Medicine.*

THOMAS B. HORAN, M.D.,
Secretary of Staff,
St. Luke's Hospital.

REPORTS OF MEETINGS

GREATER BOSTON MEDICAL SOCIETY

A meeting of the Greater Boston Medical Society was held at the Beth Israel Hospital on Tuesday evening, February 2, Dr. Henry A. Kontoff presiding. A series of papers was presented by Dr. Abraham Myerson, director of research at the Boston State Hospital, and his associates, the general topic being "The Autonomic Pharmacology of the Human Being." Dr. Myerson spoke briefly about the role of sympathin and acetylcholine in the activity of the autonomic nervous system. Animal experimentation

has shown that impulses are mediated across the synapse in both the sympathetic and parasympathetic systems by means of acetylcholine. The sympathetic nerve endings in the tissues liberate a hormone, "sympathin", which causes the response of the tissue cells. The parasympathetic nerve endings in tissue liberate a different hormone, "acetylcholine", which produces the responses characteristic of activation by this system. Certain substances known as esterases, which influence the action of these hormones, are existent in the tissues themselves. Choline esterase rapidly destroys acetylcholine by hydrolysis and checks its action, thus making the effect of parasympathetic stimulation intermittent. Most tissues possess an innervation from both the sympathetic and parasympathetic systems, which are opposed in effect, and which result in a balanced activity. There are some tissues, however, which do not possess this double innervation, and in which the existence of esterases are the only means of establishing a functional balance. The ciliary muscles of the eye were cited as an example of tissue in which there is only parasympathetic innervation.

The anatomic relations of nervous structures are not a guarantee of chemical relation. Several glands are innervated by nerves that are anatomically members of the sympathetic nervous system, although acetylcholine is liberated at their endings. The sweat gland in the human being is an example of a gland so innervated by nerve fibers that are anatomically sympathetic in type, although they are stimulated only by acetylcholine, and drugs mimicking or paralyzing the action of acetylcholine causing activity or paralysis of the sweat glands.

Various drugs that stimulate or paralyze the sympathetic or parasympathetic systems have been discovered. Mecholyl (acetyl-beta-methycholine chloride) was used by Dr. Myerson and his associates as a parasympathetic substance, and benzedrine sulfate (beta-phenyl-isopropylamine sulfate) as a sympathetic stimulant. Atropine was used to check the activity of mecholyl and the parasympathetic system, which it does by changing the reacting cell, and to enhance the effect of the sympathetic system as stimulated by benzedrine. The latter end is secured because of the removal of the influences of the antagonistic parasympathetic impulses. Prostigmin and physostigmin were used to enhance the effect of mecholyl or to obtain parasympathetic stimulation, since these drugs inhibit the activity of the esterases that usually destroy acetylcholine and diminish or curtail the activity of the parasympathetic system.

Dr. Myerson stated that some disorders in human beings may be due to the existence of too much or too little esterase in the tissues rather than to an abnormality of the sympathetic or parasympathetic systems. As a possible example of such disorder, he cited presbyopia. The administration of prostigmin to a presbyopic individual markedly enhances the ability of accommodation, although its mode of action is merely the inhibition of tissue esterase.

Dr. Julius Loman spoke on the effects of mecholyl and benzedrine on the blood pressure, pulse rate and sweat glands. The studies were performed on patients in the Boston State Hospital, who served as admirable subjects, since they were physiologically healthy and extremely docile. Dr. Loman found that mecholyl caused a transient drop in the blood pressure and an increase in the pulse rate in most cases. Rarely, there was an immediate transient slowing of the pulse followed by an increase in rate. In some cases, the pulse showed a secondary fall. The previous administration of prostigmin greatly increased the effects of mecholyl, while atropine almost completely prevented the mecholyl response. Benzedrine produced a prolonged elevation of blood pressure, while the pulse rate was only slightly affected. Atropine exerted a marked synergistic effect on benzedrine, while the simultaneous administration of benzedrine and mecholyl caused a transient fall in blood pressure followed by a prolonged increase. In patients in whom the blood pressure had fallen after the administration of amytal, benzedrine caused a prolonged and steady increase toward and above normal. Mecholyl produced flushing, sweating, salivation and rhinorrhea, which manifestations were increased in degree by the administration of prostigmin, and checked by atropine. Intracutaneous injections of mecholyl in high dilutions caused localized sweating in the region of the injection.

Dr. Max Rinkel presented findings on the effect on the gastric secretions of the drugs cited above. Mecholyl was found to stimulate the production of mucin, to increase the secretion of gastric juice and to inhibit the production of hydrochloric acid and pepsinogen, thus producing a copious alkaline gastric juice. Benzedrine slightly diminished or did not affect the amount of gastric juice, but it definitely and regularly increased the free hydrochloric acid and the pepsinogenic activity. Prostigmin increased the response to mecholyl, while atropine blocked it.

Dr. Max Ritvo presented a paper on the importance of the autonomic nervous effects in x-ray examinations of the gastrointestinal tract. Stimulation of the parasympathetic nervous system causes an increase in tone and peristaltic activity and a tendency toward spasticity of the gastrointestinal tract, while sympathetic stimulation produces opposite effects. Emotions cause a great variation in the activity of the stomach and intestines and, coupled with many other factors, may cause great difficulty in roentgen examinations. Diminished tone and peristalsis occasionally interfere greatly with the examination of the stomach and duodenum. Mecholyl was found to remedy this atony and lack of peristalsis, although it also caused unpleasant rhinorrhea, salivation and sweating. It is not used for routine purposes because of these features. Physostigmin, however, was found to be efficient in increasing gastric activity without the production of unpleasant reactions, and has proved of value in fluoroscopic examinations.

Troublesome spasm in the stomach and intestines was found to be relieved in a short time by the oral administration of benzedrine without the occurrence of important side reactions. Atropine was found to increase the spasm of the colon.

Benzedrine was found to abolish the emptying reflex of the gall bladder for a period of some two hours after its administration.

Dr. William Dameshek spoke of the effect of such drugs on the heart. Mecholyl was found to cause a marked increase in the P-R interval, which increase may be so marked that the P wave becomes involved in the preceding T wave. In some instances, this drug may cause heart block. Its effects were blocked by atropine. Prostigmin produced slowing of the heart, and in one or two instances a subsequent injection of mecholyl caused cardiac collapse with a period of asystole. Mecholyl acted on the bundle of His, and stimulated the conduction of the impulse. It may also act directly on the cardiac muscle, and stimulate the sympathetic system by its action on the synapse. Benzedrine had no effect on the electrocardiogram, although the pulse rate was diminished as a secondary effect of the elevation of blood pressure that it produced.

Dr. Boris Greenberg described the effect of mecholyl in cystometric studies. Neither mecholyl nor prostigmin administered alone had any effect on the gall bladder, although the simultaneous administration of these drugs caused rapid contraction and trabeculation of the wall.

Dr. Myerson summarized the findings previously presented, and suggested the possibility of therapeutic applications of the various drugs described. For example, the maintenance of an alkaline gastric juice by the use of mecholyl may be of value in the treatment of gastric ulcer, and it is possible to control the blood pressure by iontophoresis of mecholyl.

HARVARD MEDICAL SOCIETY

A meeting of the Harvard Medical Society was held at the Peter Bent Brigham Hospital on March 9, Dr. Robert T. Monroe presiding.

The medical case was presented by Dr. Arthur J. Hadler. A 55 year old Italian housewife had suffered an attack of pneumonia 6 years previously and had been in poor health since that time. Her local physician had treated her with iron compounds administered orally for 1 year, without improvement. She was then given iron and liver therapy for 1 year with some degree of improvement. She was first seen at the Peter Bent Brigham Hospital in 1934, at which time she was found to have a normocytic anemia with a red blood cell count of 2,280,000 and a hemoglobin of 49 per cent (Sahli). In spite of large and frequently administered doses of liver, numerous transfusions, large amounts of iron and occasional doses of ventriculin, a persistent anemia of marked degree persisted. She experienced frequent bouts of furunculosis, otitis media and bronchopneumonia, which necessitated her admission to the hospital. Laboratory studies showed a consistently elevated icteric index, ranging from 15 to 70. The clotting time, bleeding time and fragility of the erythrocytes were within normal limits. Stools and urine examinations were negative. A sternal biopsy had been performed in 1935 and showed a marked hyperplasia of the erythrocytic elements. Recently a lymph node was removed from her neck for histologic examination and a destruction of the normal elements by massive infiltration of lymphocytes, some of which had invaded the capsule, was revealed. There were occasional giant cells in sarcoid-like arrangement. A pathological diagnosis of lymphoma, with sarcoid reaction, was made.

Spray x-ray therapy to the abdomen was given without benefit, and there was a leukopenic reaction. The white blood cell count was usually between 4,000 and 5,000. On her present admission, the red count was 940,000 and the hemoglobin 15 per cent. These values rapidly fell to 540,000 and 13 per cent. She was given iron ascorbate intravenously, with a reticulocyte response of 13 per cent. The diagnosis of aleukemic leukemia was made.

Dr. Dale G. F. Friend commented on the compound used in the most recent therapy of this patient with such striking results. Iron ascorbic acid was first described and used by German investigators and is produced by the introduction of a ferrous atom into the molecule of ascorbic acid. It is a purple-blue powder which is very soluble in water, nontoxic and suitable for intravenous administration. It contains 31 per cent iron, which is held in the reduced state by the ascorbic acid. Reduced iron compounds have been found to be very active in the treatment of certain anemias. The compound has been used by the French in the treatment of carcinoma but has never before been used in anemia therapy.

The surgical case was presented by Dr. James B. Blodgett. A 62 year old, white male entered the hospital with the complaints of weakness and weight loss of 7 weeks' duration. He had had diarrhea for several weeks, and had remained in bed for 8 days before entry because of extreme asthenia. There was a history of renal stone 20 years previously and of the passage of foul urine on two occasions, the first, one year previously, and the last, 6 weeks before entry. Physical examination showed a high left diaphragm, and laboratory studies revealed 10 to 20 white blood cells per high power field in the urine and a moderate secondary anemia. Pyelography showed a ureteral stone. Operation was performed, and a perinephric abscess and a pyonephrosis were drained. The postoperative course was satisfactory. Dr. Harrison remarked that long-standing infection was often the cause of a low-grade secondary anemia, as evidenced by this patient.

Dr. William Dameshek delivered the paper of the evening on the subject, "The Diagnostic Value and

the Limitations of the Sternal Bone Marrow Biopsy." The various cells of the blood enter the circulation from the blood-forming organs, and the number and differential relations noted in the peripheral blood depend on factors governing the development and release of these cells from their sites of formation. The blood picture may not be an adequate indication of the conditions existent in the bone marrow, as is exemplified by the hyperplastic marrows associated with pernicious anemia and agranulocytosis. An occasional case of blood disease cannot be correctly diagnosed from a study of the peripheral blood, and a marrow biopsy in such cases proves of inestimable value.

Bone-marrow biopsies were first performed in 1908 by an Italian worker, Ghedini, who removed portions of the tibial marrow. Several German workers performed similar studies in 1921, and Peabody in 1925 and 1926 utilized this method to study the bone marrow in cases of pernicious anemia before and after liver therapy. Tibial biopsies are difficult to perform, however, and normal tibial marrow is entirely fatty. Seyfarth introduced the sternal biopsy in 1923, making marrow biopsies relatively simple and giving impetus to the study of marrow changes associated with abnormalities of the peripheral blood. Arinkin in 1929 introduced a method of aspirating the content of the sternal marrow cavity by puncture with a hollow needle, a procedure extremely easy to perform. The material obtained by such aspiration technic is not so satisfactory as that obtained by trephining and curettement.

Since 1928 Dr. Dameshek has performed some 200 sternal biopsies by means of the trephine technic, which he described in detail. The procedure is carried out with strict asepsis, and local novocain anesthesia is employed. An incision is made in the skin overlying the sternum at the level of the second and third intercostal spaces, and the skin is retracted. The periosteum is incised and retracted, and a trephine hole, 5 millimeters in diameter, is made in the anterior table of the sternum. The bone and marrow so obtained are fixed in Zenker's solution, and marrow obtained with a small curette is smeared directly on clean glass slides. Sections are made of the Zenker's fixed tissue and are stained with eosinmethylene blue. These sections are of value in revealing the general topography of the marrow, its cellularity and the presence of islands of primitive cells. The smears are treated with either Giemsa's or Wright's stain and are valuable in a study of the exact morphology of cells and of the differential counts.

Sternal bone marrow punctures were performed in 20 cases and were compared with the trephine method in the same group of cases by means of differential counts and careful examination of the materials obtained. The trephine method was found to be far superior to the puncture method, since only a relatively small number of the primitive, nucleated red cells were obtained by the puncture, most of the material withdrawn being blood. Lack of cellularity in the puncture preparations might be of no significance regarding the cellularity of the marrow itself.

Dr. Dameshek described a series of very interesting cases in which sternal marrow biopsy had been of inestimable value in establishing the diagnoses, illustrating each case with several lantern slides of the biopsy material. The importance of the diagnostic triad of anemia, leukopenia and thrombopenia was stressed, and it was pointed out that these features could be associated with either a "full" or an "empty" bone marrow and thus may be due to one of many diverse disorders. It is in cases presenting this triad that bone-marrow biopsy has been found to be especially useful. Studies of the marrow in cases of pernicious anemia before and after liver therapy were described. Before therapy the marrow was crowded with very primitive members of the erythrocytic series (erythrogones) and megaloblasts. There was an associated hyperplasia of the granulocytic cells with the presence of many abnormal forms. Large numbers of typical lymphocytes were also present. After the administration of liver extract there were rapid disappearance of the erythrogones and megaloblasts with their conversion to normoblasts, a disappearance of the abnormal granulocytes and lymphocytes, and an increase in the number of megakaryocytes. The megaloblastic bone marrow of pernicious anemia is another expression of the state of liver deficiency.

The macrocytosis of liver disease was found to be a normoblastic type of reaction, the macrocytes developing because of the failure of the normoblasts to shed their cytoplasm completely.

There are definite limitations of the method since only a very small amount of tissue is removed, which may not come from a representative portion of the sternum. The tissue so obtained may not be satisfactory for diagnosis, and a wrong interpretation may be made.

Dr. Henry Christian remarked that the study of the bone marrow was, for many years, regarded as more satisfactory than the study of the blood, because of the inadequacy of stains for blood cells. With the development of the Wright stain, attention was concentrated on the blood, and marrow study was neglected except at autopsy. The value of marrow biopsy is now beginning to be realized, and this method should prove of great aid in clarifying blood diseases.

Dr. Robert T. Monroe remarked that, at the Peter Bent Brigham Hospital, sternal marrow biopsy had not aided in the diagnosis of any case that could not be diagnosed by careful study of the peripheral blood.

In his concluding remarks, Dr. Dameshek stressed the fact that the hematologist should certainly be his own clinician, might well be his own surgeon and should, by preference, be his own microscopist.

BOSTON PATHOLOGICAL SOCIETY

A meeting of the Boston Pathological Society was held at the Children's Hospital on March 19, Dr. J. Beach Hazard presiding.

A case of granulosal cell tumor of the ovary was presented by Dr. Warren E. Wheeler, Dr. Harold Johnson, and Dr. Ira T. Nathanson. The patient, a 13 months old female infant, was brought to the hospital because of vaginal bleeding of 1 day's duration. She had been well until 5 months before entry when gradual enlargement of the breasts, abdomen, and genitalia was noted. Physical examination on entry revealed a well-developed, and nourished white female infant weighing 23 pounds. Fine hair was present in the axillae and on the pubes. The breasts were slightly enlarged, and tender, and rectal examination revealed enlargement of the uterus and cervix. The umbilicus was protuberant. A large, nonmovable, nontender mass was present in the lower abdomen. Intravenous pyelography showed lateral displacement of the right ureter. Operation was performed, and a large cystic mass associated with the right ovary was removed. This mass measured 11.5 by 15 by 12 centimeters and contained 750 cubic centimeters of clear amber fluid. Two thirds of the mass was composed of a single large cyst, into which protruded numerous pedunculated masses of pale yellow tissue. The remainder of the tumor was firm, yellow to yellow-grey in color, and contained numerous small cysts ranging from 0.1 to 3 centimeters in diameter. Histologically the tumor was composed of large epithelioid cells with scant cytoplasm and very numerous mitotic figures. Tumor cells were found extending along the peritoneal surface of the pedicle. Assay of the urine revealed 120 mouse units of estrogenic substance per liter, an amount approximately equal to that excreted by an adult female except at the time of ovulation. The cyst fluid contained 3,000 mouse units of estrogenic substance per liter, and qualitative assay of the tumor yielded estrogenic substance. Normally no estrin can be recovered from the urine of children under the age of 7 years, and between the ages of 7 and 13 years the output of this substance is between 24 and 72 mouse units per 24 hours. This patient was believed to be the youngest individual on record to exhibit menstruation.

Dr. S. B. Wolbach delivered the paper of the evening on the subject, "Processes Antecedent to Tumor Formation Induced by Certain Carcinogenic Chemicals." Although certain carcinogenic substances are related to estrogenic substances and cholesterol, Dr. Wolbach believes that the concept of a disturbance of cholesterol metabolism in the human body with the production of carcinogenic substances in the organism is without foundation, and improbable. Three carcinogenic agents have been investigated, and all three have been found to be destructive substances which produce damage to the tissues with subsequent proliferative response. There is no evidence of direct stimulation of cells. Slides were shown illustrating the various changes occurring in tissues adjacent to implanted pellets of dibenzanthracene. The first reaction was inflammation. This was followed by a proliferative response on the part of the damaged cells, which were no longer destroyed by the irritant. These cells had undergone some modification which enabled them to resist the previously destructive substances. Finally, a true malignant tumor was formed with atypical and multiple mitotic figures. The maximum reaction always occurred in those cells most active in the reparative processes, which, in the subcutaneous tissues, were the fibroblasts.

Repeated applications of carcinogenic substances on the skin of mice produced ulceration and chronic inflammation, which was followed by attempts at repair with proliferation of the hair follicles and downgrowth of epithelium. With the continuation of the applications, marked keratinization occurred, and multiple mitoses appeared. There was invasion of the underlying muscle bundles, and the development of a true malignant tumor. In this instance also there was no evidence of any growth-stimulating property of the carcinogenic substance, which acted merely as a chronic irritant producing a reparative and proliferative response.

Studies of the effect of amidotoluol on the livers of rats have shown that the proliferative response of the bile ducts is preceded by swelling, vacuolization, and death of the periportal liver cells with resultant disruption of the liver columns. There is subsequent regeneration of the bile ducts, in an attempt to reestablish continuity with the liver cells, and regeneration of the liver cells, which show many mitotic figures, also occurs. If these processes are continued for a long enough period of time, the cells take on the characteristics of true malignancy, and tumors develop. Different regions in the same liver show different histologic pictures, and there is evidence of some acquired resistance by the production of islets of normal regenerated tissue surrounded by fibrous tissue.

Dr. Wolbach has been convinced by his studies that the important factor is not the nature of the chemical substance employed, but the response of the cell to toxic substances, in an effort to repair damage. He presented this theory as opposed to the concept that certain chemicals cause a direct stimulation of cells to tumor formation.

Dr. M. J. Shear stated that some substances produce chronic inflammation for long periods of time but never carcinoma, while chemically closely related substances produce carcinoma in a relatively short time. Dr. Wolbach replied that the agents employed must not be too strong or too weak, or the results obtained cannot be compared with those obtained with other substances. In order to accept the concept of actual stimulation of tumor formation, a chemical must be found which will cause the development of a tumor without first causing injury. A complete understanding of the problem will be achieved only when a chemical is discovered which will stimulate the biochemical systems concerned with growth, and which will stop those systems concerned with degeneration.

NOTICES

REMOVAL

MARION AGNES D. WILKINSON, M.D., announces the removal of her office to 160 Park Street, West Roxbury.

BOSTON PATHOLOGICAL SOCIETY

A meeting of the Boston Pathological Society will be held at the Mallory Institute, City Hospital, on Wednesday, May 26, at 8:00 p. m.

PROGRAM

1. Clinical and Pathological Aspects of Boeck's Sarcoid. Dr. D. A. Nickerson.
2. Primary Multiocular Aneurysm of the Aorta. Dr. R. Crane.
3. Correlation of the Histological Picture with Age of Cardiac Infarcts. Dr. K. L. Mallory.
4. Color Photography with the Kodachrome Process. Dr. K. L. Mallory.

Physicians and medical students are cordially invited to attend.

S. C. DALRYMPLE, M.D., *Secretary.*

MASSACHUSETTS MEMORIAL HOSPITALS

There will be a luncheon meeting of the Surgical Section in the Aid Association Room, ground floor, Talbot Memorial, 82 East Concord Street, Boston, on Friday, May 21, at 12 noon.

Dr. David B. Stearns will present a paper on "Contusions of the Kidney."

Dr. Ensio K. F. Ronka will present a case report "Arteriectomy for Arteriosclerosis."

Surgical deaths for the month of March will be discussed.

MILO C. GREEN, M.D., *Secretary.*

NEW ENGLAND PHYSICAL THERAPY SOCIETY

The annual meeting of the New England Physical Therapy Society will be held at the Hotel Victoria, Boston, on Wednesday evening, May 26.

The Council will meet at 6:00 p. m.; round table dinner at 6:30 p. m.

PROGRAM

Promptly at 8:00 p. m.

1. Reports of officers and committees.
2. Election of officers.

SCIENTIFIC PROGRAM

1. X-ray and Radium Therapy. Charles Whelan, M.D., Boston, physician-in-charge of radium therapy, Carney Hospital; visiting roentgenologist, Quincy City Hospital.
2. Question Period.

All members of the medical profession are cordially invited to attend.

WILLIAM D. MCFEE, M.D., *Secretary.*

41 Bay State Road,
Boston.

ACADEMY OF PHYSICAL MEDICINE

The special business meeting of the Academy of Physical Medicine, scheduled for May 19, has been postponed to 5:30 p. m., Wednesday, May 26, at the office of the secretary-treasurer, 144 Commonwealth Avenue, Boston.

HERMAN A. OSGOOD, M.D.,
Secretary-Treasurer.

BOSTON CITY HOSPITAL

A clinical meeting of the staff of the Boston City Hospital will be held in the Thorndike Amphitheater, Boston City Hospital, on Saturday, May 22, at 10:00 a. m.

PROGRAM

1. The Study of Alcoholism at the Boston City Hospital. Dr. Merrill Moore.
2. A New Series of Anticonvulsants, Tested on Animals. Dr. H. Houston Merritt and Dr. Tracy J. Putnam.
3. Epilepsy—A Paroxysmal Cerebral Dysrhythmia. Dr. William G. Lennox, Dr. F. A. Gibbs and E. H. Gibbs.
4. Migraine and Its Treatment. Dr. Theodore J. C. von Storch.
5. The Results of Treatment of Athetosis and Dystonia by Section of the Extrapyramidal Tracts. Dr. Tracy J. Putnam.

Committee on Hospital Clinics.

SOCIETY MEETINGS, CONGRESSES AND CONFERENCES

CALENDAR OF BOSTON DISTRICT FOR THE WEEK BEGINNING MONDAY, MAY 24

Monday, May 24—

*8 p. m. Lecture on alcoholism, Miss Mabel R. Wilson, in the amphitheater of the Mallory Institute of Pathology, 784 Massachusetts Avenue, Boston.

Tuesday, May 25—

*9 a. m. - 10 a. m. Boston Dispensary, 25 Bennet Street, Boston. X-Ray Demonstration. Dr. Alice Ettinger.

11:30 a. m. Massachusetts General Hospital. Eye Nerve Conference. Out patient department.

Wednesday, May 26—

8 a. m. Massachusetts General Hospital. Grand rounds. Orthopedic department.

*9 a. m. - 10 a. m. Boston Dispensary, 25 Bennet Street, Boston. Hospital case presentation. Dr. S. J. Thannhauser.

†12 m. Clinicopathological conference. Children's Hospital amphitheater.

4 p. m. - 5 p. m. Surgical pathological conference. Dr. Cutler and Dr. Wolbach, Peter Bent Brigham Hospital.

5:30 p. m. Academy of Physical Medicine, 144 Commonwealth Avenue, Boston.

*8 p. m. New England Physical Therapy Society. Hotel Victoria, Boston.

*8 p. m. Boston Pathological Society. Mallory Institute, Boston City Hospital.

Thursday, May 27—

9 a. m. Massachusetts General Hospital. Surgical grand rounds.

*9 a. m. - 10 a. m. Boston Dispensary, 25 Bennet Street, Boston. Social service case presentation. Mrs. H. B. Hooker, Miss Elizabeth Grundy.

9:15 a. m. Massachusetts General Hospital. Neurological conference. Ether Dome.

12 m. Massachusetts General Hospital. Clinicopathological conference.

Friday, May 28—

*9 a. m. - 10 a. m. Boston Dispensary, 25 Bennet Street, Boston. The Effects of Emotion on the Body. Dr. Walter B. Cannon.

10 a. m. Massachusetts General Hospital. Fracture rounds.

12 m. Massachusetts General Hospital. Clinical meeting of the staff of the Children's Medical Service. Ether Dome.

Saturday, May 29—

*9 a. m. - 10 a. m. Boston Dispensary, 25 Bennet Street, Boston. Hospital case presentation. Dr. S. J. Thannhauser.

*10 a. m. - 12 m. Staff rounds at the Peter Bent Brigham Hospital. Conducted by Dr. Henry A. Christian.

*Open to the medical profession.
†Open to Fellows of the Massachusetts Medical Society.

May 20—New England Women's Medical Society, 7 p. m., Hotel Puritan, Boston.

May 21—Massachusetts Memorial Hospitals. Luncheon meeting of the Surgical Section. Page 910.

May 22—Boston City Hospital, Clinical Meeting of the Staff. Page 910.

May 26—New England Physical Therapy Society. Page 910.

May 26—Academy of Physical Medicine. Page 910.

May 26—Boston Pathological Society. Page 910.

June 1, 2 and 3—Annual meeting, Massachusetts Medical Society, Hotel Bradford, Boston.

June 7—American Medical Golfers Play in Atlantic City. Page 582, issue of April 1.

June 7 and 8—American Heart Association. Page 769, issue of April 29.

June 7-11—American Medical Association. Atlantic City. Page 709, issue of April 22.

June 8—The American Neisserian Medical Society. Page 489, issue of March 18.

June 8 and 9—American Board of Obstetrics and Gynecology. Page 78, issue of January 14.

June 11-18—Catholic Hospital Association. Page 488, issue of March 18.

June 24—Pentucket Association of Physicians. 8:30 p. m. at "Duck In."

July 6-11—Fifth International Congress of Hospitals. Page 37, issue of January 7.

September 13-17—Fifth International Congress of Radiology. Page 709, issue of April 22.

October 5-8—American Public Health Association meeting. New York City.

October 9—American Board of Ophthalmology, Chicago. Page 722, issue of April 22.

October 19, 20, 21—Academy of Physical Medicine. Page 723, issue of April 22.

October 25-29—American College of Surgeons. Chicago, Illinois.

DISTRICT MEDICAL SOCIETY

PLYMOUTH DISTRICT MEDICAL SOCIETY

May 20—11 a. m. Lakeville State Sanatorium.

FRED F. WEINER, M.D., Secretary.
231 Main Street, Brockton.

BOOK REVIEWS

Eugenical Sterilization. A Reorientation of the Problem. By the Committee of the American Neurological Association for the Investigation of Eugenical Sterilization. 211 pp. New York: The Macmillan Company. $3.00.

For many years there has been a growing belief that somehow or other the government should interest itself in the problem of eugenics. As a result, a great many states and some countries have put laws upon their books authorizing some form of sterilization. To date, the matter has not been submitted to careful scientific scrutiny.

In 1934, a Committee was appointed by the American Neurological Association to investigate the matter. The report was presented to and accepted by the American Neurological Association at its annual meeting in 1935. From the Foreword of this book we find, "It had such an enthusiastic reception that it was felt advisable to publish it in a more permanent form and make it available to the general public." Accordingly, the book under consideration has just been presented to the public.

A detailed analysis of the laws authorizing sterilization is presented. Then the various arguments for sterilization are considered and taken up in order. The first of these has to do with the alleged increase in insanity, feeblemindedness, epilepsy, pauperism, alcoholism, and certain forms of criminality. Much material is brought together tending to refute this belief, and it would appear from the authors' study that there is no real justification for any such conclusion.

Next is considered the frequent statement that defective people propagate at a greater rate than the normal population. Everywhere in the popular literature on the subject the large families of the feebleminded, of the insane, and of the pauper class are stressed, and it is pointed out that the general birth rate, especially for the people of the higher levels, is declining. Here again the authors do not find this belief to be supported by available data. In fact, the reverse seems to be true. Nervous and mental disorders are so disabling in their effect that they tend to limit rather than to increase propagation.

The argument that these conditions are fundamentally and mainly hereditary is next considered. An excellent chapter is devoted to a critique of various researches on inheritance of mental diseases. As a result the role of heredity is reduced to a minimum.

This introduces the last argument, namely, that the proponents of eugenics usually stress the environment as, on the whole, of much less importance than the germ plasm. The authors bring forward a great deal of material to show the importance of environment as a great factor in nervous and mental diseases.

A definite attack is made upon the theory of polymorphism, and much information is given tending to show that there is no hereditary influence which has a general blighting effect upon the nervous systems of posterity.

It is recommended that a permanent committee be appointed which shall take steps necessary for the organization of research in these directions. The recommendations of the committee end as follows:

"The Committee wishes to stress the fact which the diligent reader of the report will have noted; to wit, that in large measure marriage is a selective agency operating in a eugenic way. The barriers of marriage against unwise procreation might

well be strengthened by appropriate and early legislation.

"Furthermore, it is to be emphasized that no great or radical change in the complexion of society can be expected from any such sterilization program as we recommend, nor from any justifiable legislation. We do not believe that society needs to hurry into a program based on fear and propaganda. Although the problem of mental disease and defectiveness is enormous, there exists no new social or biological emergency."

There follows an ample bibliography.

The book is vigorously written, and if one follows its reasoning there appears to be little hope of the improvement of society through eugenical sterilization. One can have little doubt as to the attitude of the committee. Since four out of five on the committee are Boston men, it perhaps represents a Boston point of view. Occasionally, like Dr. Johnson, the authors appear to "talk for victory." This when they say that the Kansas law authorizing sterilization is perhaps sadistic in motivation, and "it is obvious that the term insanity means nothing from a psychiatric point of view." The fear is later expressed that the laws are discriminatory in that they tend to act on individuals in state hospitals. A breath from Russia?

Perhaps too little credit is given for the idealism which after all lies back of most of the effort in this direction. From the committee's study it would appear that eugenical sterilization is not a method by which it can be hoped to improve society. This, however, should not deter forward-looking individuals in their hope that the effects of bad breeding can be ameliorated and that the public may be made conscious of the possibilities of good breeding among human beings.

A Dissertation on the Sensible and Irritable Parts of Animals. Albrecht Von Haller. 49 pp. Baltimore: The Johns Hopkins Press. 1936. $1.00.

In 1752 Albrecht Von Haller made a very important contribution to our knowledge of muscular physiology in a paper read at Goettingen. This paper was a detailed account of a large number of experiments which he had done on both animals and human beings in order to investigate the fundamental properties of sensibility and irritability. Although his conclusions were not entirely new, his scientific method of examination and the clear-cut way in which he reasoned from his observations made his contribution an outstanding one. He clearly established the difference between sensibility and irritability, but failed, unfortunately, to notice reflex action, which would have greatly changed some of his conclusions, had he been familiar with this fundamental principle. By his careful work, moreover, he started other investigators along similar lines of endeavor. His book, first published in Latin in 1753, was translated into French in 1755 and then into English in the same year.

All of the publications are not of easy access to students and for this reason the English translation has been republished in a convenient form as one of the reprints of medical classics issued by the Institute of the History of Medicine, Johns Hopkins University. There is a brief introduction evaluating this contribution of Von Haller, but, unfortunately, an index is missing. This book, as well as others in the same series, is excellently printed and to be had at a very reasonable price.

Remington's Practice of Pharmacy. A Treatise Intended for the Use of Pharmacists and Physicians and As a Textbook for Students. E. Fullerton Cook and Charles H. LaWall. Eighth Edition. 2162 pp. Philadelphia and London: J. B. Lippincott Company. $10.00.

This large volume includes, apparently, the content of a course leading to a degree in Pharmacy. To the medical reviewer it is impressive to survey the field and to recognize its magnitude. It describes the technical operations of pharmacy with the applications of physics and chemistry involved, nearly all substances and preparations of the pharmacopoeias and formularies, chemical and biological assays, manufacturing methods and many practical methods of professional procedure. To the physician, however, the work can hardly be of great service since our many books on medical pharmacology and therapeutics are much more appropriate to his needs. Still, it is satisfactory to recognize that the registered pharmacist has such a fund of special information and that such an excellent book is available for reference.

Urological Roentgenology. A Manual for Students and Practitioners. Miley B. Wesson and Howard E. Ruggles. 269 pp. Philadelphia: Lea & Febiger. $5.00.

This short book of 269 pages is well illustrated and contains practically all the pathologic urologic entities seen by the roentgenologist. However, throughout the book, the reviewer obtains the feeling that the author is citing opinion for fact. A great number of statements are made that could easily be debated, and some statements do not appear to be too exact or scientific.

In discussing the contraindications to intravenous pyelography, the author states that patients in pregnancy and those having active tuberculosis are particularly prone to reactions. The reviewer is of the opinion that this is not an accurate statement, for intravenous pyelography is constantly being used in lying-in clinics and in sanatoria all over the country with no more reactions than one ordinarily sees in any other type of case. One can also doubt the statement that "Aberrant blood vessels have generally been considered responsible for most cases of hydronephrosis." The statement made in discussing simple cysts that "A gradual increase in filling defect on repeated pyelograms is

pathognomonic of a cyst" is a far cry from accuracy, since this may be equally true of tumor.

It is just such types of statements that run throughout the book and seem to detract from its scientific value. A bibliography is appended.

One Hour of Medical History. Benjamin Spector. Volume V. 155 pp. Boston: The Beacon Press, Inc.

For five years the students of Tufts College Medical School, under the direction of Dr. Benjamin Spector, have given a pageant to commemorate outstanding events in medical history. The material presented in the 1936 pageant is incorporated in the present little volume.

The period covered is the first three centuries of the medical history of Massachusetts, with special reference to the earlier portion. Not only doctors but the Indian Medicine Man, Governors and ministers are included; in those days laymen were not infrequently influential in directing the trend of medical practice. Each episode deals with a significant event in the life of the character who is presented. There is a graceful little preface by Dr. Henry Viets and a description by James F. Ballard of the historical bibliographic demonstration which was presented at the time of the pageant.

It is not unlikely that this method of setting forth the outstanding events of medical history leaves a deeper impression upon the reader than many pages of dry historical facts.

Patient and Doctor. Sir Henry B. Brackenbury. 280 pp. London: Hodder and Stoughton.

The author has presented a very interesting discussion of medical services in Great Britain. It has, however, more than local interest. The section on the history of medicine, drawing attention to the development of medical ideals, is presented in an unusual form. Although the discussion throughout the book bears directly upon medical problems in Great Britain they are fundamentally the same problems that confront the medical profession everywhere and, therefore, the general thesis is of significance outside of Great Britain. His ideas may be summarized by quoting his conclusions as follows:

> (1) The foundation of the doctor's equipment must be scientific in the strictest and fullest sense, and must be constantly based upon both clinical and laboratory research.
>
> (2) The outlook of the doctor must be characterized by "wholeness" with regard to both the complete personality of the patient--body and psyche—, the entire environment of the patient, and the three aspects of medicine—cure, prevention, perfection.
>
> (3) The fundamental characteristics of the relation between patient and doctor must include:
>
> (a) Complete freedom, both as regards the nature of the advice and treatment that the doctor proposes to give and as regards choice of doctor by patient and patient by doctor at any time;
>
> (b) Confidence by the patient that the doctor is his *own* doctor, whose duties are primarily directed toward the patient's interests and welfare and nothing else.
>
> (4) The comprehensive and far-reaching nature of the work of the doctor in the preventive and communal sphere must be recognized and practically utilized.

The book is well worth reading.

The Medical Clinics of North America. Volume 20, Number 2, September, 1936. St. Louis Number. 685 pp. Philadelphia and London: W. B. Saunders Company.

The leading feature of this volume of the well-known Medical Clinics is the "Endocrine Symposium" including the following "clinics": Borderline Endocrine Disturbances, Endocrine Obesity, The Treatment of Pituitary Insufficiency and Pituitary Hyperfunction, Diagnosis and Treatment of Hyperinsulinism. The remainder of the volume is taken up with discussions of miscellaneous topics: encephalitis, silicosis, uremia, neuroses and psychoses, and so forth. As is common in these volumes, some of the articles seem hastily put together, cursory, and slipshod, whereas others are distinguished by careful writing and much practical value. The symposium on the endocrines is incomplete, lacks integration, is cursory in some spots and too detailed in others. Most of the other articles are quite practical and contain much information that is otherwise difficult for the busy general practitioner to assemble.

Allergic Diseases. Their Diagnosis and Treatment. Ray M. Balyeat, assisted by Ralph Bowen. Fourth Edition, Revised and Enlarged. 516 pp. Philadelphia: F. A. Davis Company. $6.00.

This book is now presented in its fourth edition. The paper, print, arrangement of text and illustrations are good. The work represents fifteen years of study by the author. His observations are based on the findings made on a group of 12,000 patients, seen at different times over periods of from two to four years. While the author's locale is Oklahoma, the climato-botanico-geographical distribution of all wind-borne and insect-borne pollens, of trees, plants and grasses and of cosmetics, paints, and so forth, is discussed. In fact, every type of irritant is recognized in its possible relation to the production of so-called allergic responses. The larger part of the book deals with hay fever and asthma. Balyeat states that the cause of most cases of hay fever and of 60 per cent of the cases of asthma is the wind-borne pollen of plants. He believes that

65 per cent of hay-fever victims become asthmatic in time.

This edition contains much of the material of the third edition, some chapters of which have been rewritten, and other new chapters on the more recent phases of allergy have been added. The allergic aspects of various syndromes other than hay fever and asthma are discussed. The greatest advances in allergic study have been made in the fields of dermatology and gastroenterology. The author has tried especially to present his subject for the practical use of the general practitioner in diagnosis and treatment.

Some space is devoted to the intratracheal introduction of iodized oil as a therapeutic measure, particularly in cases of intractable asthma. This form of treatment will undoubtedly meet with some opposition, or at least discussion. Its pharmacologic action is well recognized, but the difficulty of elimination of the oil from the respiratory tract afterward must always be borne in mind. Adrenalin and ephedrine are the author's drugs of preference for palliative treatment. The injection of small quantities of ether by rectum for acute asthmatic attacks is recommended in certain cases.

It is interesting to note the omission of one possible etiologic (and therapeutic) factor now under considerable discussion, that is, the psychic factor. No reference is made to this possibility, even in the small percentage (15 to 25 per cent) of cases of allergic disease syndromes in which specific sensitivity cannot be demonstrated. The endocrine and autonomic nervous systems are not mentioned throughout the book, although these systems must play a large part in the preparation of the "soil," that is, the individual patient's constitutional background, for reaction to what normally does not produce hay fever or asthma. In other words, the book presents hay fever, asthma and other "allergic" responses as *fully matured* syndromes, and treatment is directed toward them entirely on this basis. However, Balyeat gives the reader in this volume a satisfactorily clear and complete description of the subject of allergic disease as it is understood today. The book is recommended to the profession, and particularly to those men whose practice includes any number of these unfortunate "allergic" individuals.

Medical Classics. Compiled by Emerson Crosby Kelly. Volume I, Number I, September, 1936. 78 pp. Baltimore: The Williams & Wilkins Company.

If Volume I, Number I, of *Medical Classics* is a forecast of the future publications in quality, presentation and reproductions of drawings, gross specimens, and so forth, the periodical will meet a very definite want that many men in the active practice of medicine and surgery, as well as medical students, have felt. The policy of *Medical Classics* is stated clearly in the preface. It is to publish original articles by outstanding men of the past, in order that we of today may realize more clearly what Claude Bernard pointed out when he said, "We stand upon the intellectual shoulders of those medical giants of bygone days and, because of the help they afford us, we are able to see a little more clearly than they were able to do."

The first number presents three original articles by Sir William Paget (two on osteitis deformans and one on Paget's disease of the nipple) and a complete bibliography of his own writings. These articles emphasize the fact that an original article is always more valuable than any abstract, digest or interpretation of it by another than the author. One is impressed also with the realization that no more is known today about Paget's disease than when it was first described by the man to whom it owes its name. Paget considered osteitis deformans as inflammation of the bone-producing changes entirely different in appearance and course of development than those found in other diseases where bone is involved. His case histories are excellently presented. They show how, in the past, the physician, depending on his special senses and keen observation, understood certain disease pictures as well as we do today with all the modern diagnostic facilities. He followed his patients throughout life, during the course of their disease to death, so that his observations were based on irrefutable facts. It is particularly interesting to note this very complete "follow-up" of patients occurring in the middle of the nineteenth century, in contrast to some of the present-day presentations of cases illustrating "cures" or "end-results" at the end of a six-month or one-year period of time.

This magazine, as outlined for future publications, will bring the past into the present in a pleasing and valuable form. It promises to be a real contribution to medical literature.

Kama Sutra. The Hindu Science of Love. Mallinaga Vatsyayana. 127 pp. New York: The Medical Press of New York. $2.00.

"Kama Sutra" or "The Hindu Science of Love" is translated from the Sanskrit by Sir Richard Burton, with a section on "The Doctor as Marriage Advisor," by Max Hodan, M.D., and an introduction by Hanns Heinz Ewers.

This small volume, apparently emanating originally from Berlin, constitutes another contribution to the growing mass of pseudomedical pornographic literature, published with the transparent excuse of promoting harmony in marital relations. There is no question but that a better appreciation of the psychology of sex relations would save many a marriage from shipwreck on the rocks of incompatibility; it is a question how far this can be accomplished through the medium of the printed word. Certainly the effectiveness of any attempt is damaged by the slightest atmosphere of salacity, and salacity is the keynote of much of the contraband literature of this type.